# Article

# Risk factors for initial respiratory disease in United States' feedlots based on producer-collected daily morbidity counts

Michael W. Sanderson, David A. Dargatz, Bruce A. Wagner

**Abstract** – The incidence of initial respiratory disease was followed for 12 weeks in 122 pens of feedlot cattle, based on producer-collected daily morbidity counts. Weekly incidence density was calculated based on the number of new cases and the population at risk. Incidence density was greatest in the 1st week after arrival and decreased in following weeks. Weekly incidence rate varied between pens and over time from 0 to 27.7 cases per 100 animal weeks at risk. A negative binomial model controlling for multiple events within pens and over time was used to model effects on the number of new cases. Mixed gender groups, cattle from multiple sources and increasing distance shipped were associated with increased risk for initial respiratory morbidity. Heavier entry weight was associated with decreased morbidity risk. These factors may be useful in categorizing groups of calves into risk groups for targeted purchase and management decision making.

**Résumé – Facteurs de risque pour les maladies respiratoires initiales dans les parcs d'engraissement aux États-Unis en se basant sur le dénombrement quotidien de la morbidité recueilli par les producteurs.** L'incidence de maladie respiratoire primaire a été suivie pendant 12 semaines dans 122 enclos de bétail d'engraissement, en se basant sur le dénombrement quotidien de la morbidité recueilli par le producteur. La densité d'incidence hebdomadaire a été calculée en se basant sur le nombre de cas nouveaux et la population à risque. La densité de l'incidence était la plus importante dans la première semaine après l'arrivée et diminuait dans les semaines suivantes. Le taux d'incidence hebdomadaire varie entre les enclos et dans le temps de 0 à 27,7 cas par 100 animaux/ semaine à risque. Un modèle binominal négatif pour les événements multiples dans les enclos et dans le temps a été utilisé pour modéliser les effets sur le nombre de nouveaux cas. Les groupes de sexe mixte, le bétail provenant de sources multiples et l'accroissement de la distance de transport étaient associés à un risque accru pour la morbidité respiratoire initiale. Un poids supérieur à l'arrivée était associé à un risque réduit de morbidité. Ces facteurs peuvent être utiles dans la catégorisation des groupes de veaux en des groupes à risque pour l'achat ciblé et la prise de décisions relatives à la gestion.

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#### Introduction

**B** ovine respiratory disease (BRD) is a major cause of disease and economic loss to feedlots in North America, accounting for 70% to 80% of total morbidity and 40% to 50% of mortality (1). The majority of respiratory disease occurs in the first 45 d following arrival at the feedlot (1). Economic losses include labor and treatment costs, mortality, and decreased

Department of Clinical Sciences, 103J Mosier Hall, Kansas State University, Manhattan, Kansas, USA (Sanderson); Centers for Epidemiology and Animal Health, USDA-Animal and Plant Health Inspection Service-Veterinary Services, Fort Collins, Colorado, USA (Dargatz, Wagner).

Address all correspondence to Dr. Michael W. Sanderson; e-mail: sandersn@vet.k-state.edu

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This study was carried out with funds from the USDA:APHIS:VS Centers for Epidemiology and Animal Health as part of the National Feedlot '99 survey. daily gain and decreased percentage of cattle that grade choice. Compared with calves that never experience respiratory morbidity, morbid calves have lower average daily gains (2), although some of this difference may be overcome later in the finishing period. Additionally, calves that are not recognized as morbid but have detectable lung lesions at slaughter also have decreased weight gains (3). In the United States Department of Agriculture (USDA) Feedlot '99 study, 14.4% of cattle placed in feedlots developed BRD and the cost of medicine for treatment averaged \$12.59 (USD) (4).

performance in affected animals, including decreased average

The USDA's National Animal Health Monitoring System's Feedlot '99 study was designed to survey health and management of cattle in United States' feedlots. As part of this study, a subset of self-selected, participating feedlots voluntarily provided detailed daily health information for 1 to 3 pens of cattle from arrival to finishing.

The purpose of this analysis was to examine the incidence of respiratory disease and to identify risk factors for increased incidence of initial detection of respiratory disease during the first

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12 wk on feed among feedlot cattle in the United States. Most studies that have examined the effect of management factors on respiratory morbidity have looked at cumulative incidence of disease in the feedlot but not at individual time points. By calculating weekly incidence densities over the initial 12 wk of the study we explicitly accounted for time effects.

# Materials and methods

As part of the United States Department of Agriculture: Animal and Plant Health Inspection Service: National Animal Health Monitoring System's (USDA:APHIS:NAHMS) Feedlot '99 survey, management data were collected by using a questionnaire during a personal interview on 520 feedlots in 12 states. A stratified random sample of feedlots was selected by the USDA's National Agricultural Statistics Service (NASS) from their database of farm operations. Feedlots with the capacity to hold more than 1000 head at a single time were eligible to participate. In the 2nd phase of the Feedlot '99 survey, administered by USDA veterinary medical officers, 275 of the original 520 feedlots participated. As a part of this 2nd phase, feedlots were asked to track daily morbidity and mortality by perceived cause in 1 to 3 pens of cattle over the course of the feeding period. Morbidity and mortality data were collected in real time during the course of the feeding period. Each day during the course of the operation's regular protocol for treating morbid animals, cattle within each pen were identified as sick or dead, and specific disease categories were recorded. This tracking resulted in daily records of morbidity and mortality by perceived cause. Sick cattle were also identified as initial or repeat morbidities. Information regarding management practices specific to the individual study pens was collected for analysis of morbidity and mortality risk. Cattle in the study pens were initially placed on feed between July 23, 1999, and March 22, 2000. Placements for all quarters of the year were included, except for the 2nd quarter (April-June).

The analysis reported here is limited to the incidence of initially identified feedlot respiratory disease cases during the first 12 wk on feed. An animal that developed respiratory disease was counted during the week of its initial occurrence only and then removed from the at-risk population. Thus, individual animals could not be counted as having initial respiratory disease more than once during the study period. Reported daily counts of initial respiratory disease cases were aggregated over each week on feed to arrive at weekly counts of initial respiratory disease cases. No standard case definition for a respiratory disease case was established and identification of cases was left to the discretion of the hospital crew at each individual feedlot. Based on the initial count of cattle placed in each pen, the weekly pen population at risk was calculated for each pen by subtracting the number of weekly initial respiratory disease cases and weekly mortalities from the population at risk. Weekly initial respiratory disease counts and population at risk were used to calculate weekly incidence density of initial respiratory disease morbidity for each individual pen. A negative binomial generalized estimation equation (xtgee; Stata Statistical Software release 8.2, 2003, Stata Corporation, College Station, Texas, USA) (5) was used to account for the multiple observations within each pen and over time in the univariate and multivariable analyses of weekly count of initial respiratory disease morbidity. We initially explored a Poisson model for the data, but based on evidence of a lack of fit, as indicated by a dispersion value of 2.2 in the Poisson model, we used a negative binomial model. Candidate risk factors in the areas of feedlot management, cattle attributes, and vaccination practices were screened individually for association with weekly initial respiratory morbidity counts by pen. Variables that were associated with weekly morbidity counts at P < 0.2 in the univariate analysis were offered to a multivariable model. An autoregressive correlation matrix with a lag of 1 was specified to account for the correlation between weeks. The Huber/White/sandwich estimator was used to calculate robust standard errors for the model. Model selection was based on backward elimination of candidate variables. For each evaluation of the model, the variable with the largest Wald Chisquare *P*-value was removed. This process was repeated until all remaining variables were significantly associated with the weekly respiratory disease count (P < 0.05). Continuous variables in the model were assessed for linear effect by categorizing them into quintiles and plotting the estimated incidence rate ratios to visually evaluate linearity in the incidence rates. Variables with non-linear plots were categorized, based on apparent breakpoints in the plots and biological plausibility. Interactions between final variables in the model were assessed.

#### Results

One hundred and two of the 275 feedlots in the 2nd phase returned complete data on 122 pens of cattle. Feedlots returning pen data were from 9 of the 12 states. States (number of pens reported) included were Washington (n = 2), Idaho (n = 6), Colorado (n = 16), New Mexico (n = 1), Texas (n = 16), Kansas (n = 40), Nebraska (n = 38), Iowa (n = 2), and South Dakota (n = 1). Average cattle on feed inventory as of July 1, 1999, for the 102 participating feedlots was 10 327 head (median 6676) and ranged from 0 to 68 487 head. Yearly placements from July 1, 1998, to June 30, 1999, averaged 27 892 head (median 17 609) with a range of 395 to 165 033. The 122 pens in the study population included 20 136 cattle. Mean pen size was 165 head (median 144), with a minimum of 10 and a maximum of 569. Yearling cattle (cattle 12 to 18 mo of age) comprised 88/122 (72%) pens and calves (cattle less than 12 mo of age) 34/122 (28%) pens. Pens containing steers or heifers alone comprised 60% and 30% of all pens, respectively; 10% of pens contained steers and heifers. There were no cow or bull pens. Cattle in 95/122 (78%) of pens received an initial vaccination within 3 d of arrival at the feedlot, but cattle were revaccinated in only 33% of pens. In 105/122 (86%) pens, cattle originated from a single source, while in the remaining 17 pens, cattle originated from a mean of 2.5 different sources. Median entry weight for all cattle was 335 kg (737 lb), and the 25th and 75th percentiles were 278 kg (612 lb) and 382 kg (840 lb), respectively.

There were 1194 initial cases of respiratory disease among the cattle in the study population for a cumulative incidence of 5.9% over the course of the observation period. Individual pen cumulative incidence varied from 0 to 80% (Figure 1). Weekly incidence density rate varied among pens and over weeks from





**Figure 1.** Proportion of pens by cumulative incidence of initial respiratory disease.

0 to 27.7 cases of respiratory disease per 100 animal weeks at risk. Incidence density rates calculated by week and across pens were highest in week 1 and decreased in following weeks. The highest individual pen incidence density rate occurred in week 6.

Variables included and results of the univariate screening are reported in Table 1. In the final multilevel model, week on feed, mixed sex groups, average miles transported, and multiple source groups were associated with weekly pen initial morbidity counts. There were no significant interactions between the final model variables. Week on feed and entry weight were categorized into groups, based on Incidence Rate Ratio (IRR) plots. Morbidity risk was highest in weeks 1 to 3 and decreased through the end of the 12-week period. Mixed sex groups (heifers and steers) were at increased risk for initial respiratory morbidity (IRR = 3.7), but heifers were not at increased risk compared with steers. Mixed sex groups were also at increased risk compared with heifers, based on a post model contrast (IRR 2.9, P = 0.003). Cattle from multiple sources (IRR = 2.0) and arriving from increased distance (IRR = 1.001) were also associated with increased initial respiratory risk. Heavier entry weight was associated with decreased morbidity risk (Figure 2). Compared to cattle with entry weights below 250 kg (550 lb) cattle with entry weights between 250 and 318 kg (550 to 700 lb) tended to have less initial respiratory risk (IRR = 0.52, P = 0.09). Cattle with entry weights over 318 kg (700 lb) were less likely to experience initial respiratory morbidity (IRR = 0.18, P < 0.00). No specific vaccination practices were associated with increased or decreased initial respiratory morbidity in the final model. The final negative binomial model had a dispersion value of 1.05, indicating it was not significantly over- or under-dispersed.

## Discussion

Respiratory disease is a major disease and cause of economic loss in United States' feedlots. The pattern of respiratory disease in this study is consistent with that seen in other studies where the majority of disease cases occured in the early part of the feeding period (1). Financial losses result from treatment and labor costs, decreased weight gain, and death. Identification of



**Figure 2.** Incidence density of initial respiratory disease morbidity by week and weight category.

<250 kg

>318 kg

250-318 ka

risk factors for increased occurrence of disease is a valuable tool for feedlot management decision making. Reliable information on the impact of risk factors on expected morbidity rates for groups of cattle is useful in planning labor needs and discount or premium pricing. A negative binomial or Poisson regression model is appropriate to analyze data in the form of counts, and it has the advantage of producing coefficients that are interpretable as incidence rate ratios.

In the feedlots included in this study, longer transport distances for arriving calves was associated with an increased morbidity incidence. It seems biologically plausible that increased stress might be associated with increased time spent in transit; however, supportive data for this in cattle are rare. Warriss et al (5) conducted an experimental study involving 24 calves divided into 3 groups and hauled for 5, 10, or 15 h. Serum creatine phosphokinase activity, a measure of muscle trauma, increased in calves with increasing transport time suggesting some level of increased stress, fatigue, or both. Calves in this study hauled for 15 h also tended to have decreased hay consumption for the first 4 d after transport. Warriss et al (5) concluded that overall, 15-hour transport was little, if any, more stressful to the animals than shorter times, but the study was small and morbidity or mortality were not assessed. In a study of 105 calves hauled 3163 km (1930 miles), the calves showed increases in lipid peroxidation markers and decreases in total antioxidant capacity compared with pre-transport baseline levels (6). The authors hypothesized that these indicated increased oxidative stress and potentially increased risk for BRD. There were no control cattle with a short transport distance for comparison. In a Canadian study involving a single feedlot over a 4-year period, no difference in respiratory mortality in calves shipped longer distances was found (7). Cattle in the Canadian study were recently weaned, auction market derived calves. Most calves appear to have been commingled with multiple other sources of calves over several days during procurement. Shipping distance varied from 90 to 1326 km (55 to 808 miles).

The study reported here differs in that it assesses morbidity rather than mortality, which may account for the difference between the studies. Measurement of mortality is subject to **Table 1.** Variables tested for univariate association with the incidence of initial respiratory morbidity counts, in 122 pens of cattle on 102 feedlots. Variables with P < 0.2 were offered to a multivariable negative binomial model assessing feedlot management, cattle attributes, and vaccination practices

Factor	Percentage of pens (# pens) or Median (10th & 90th percentile)	Coefficient	<i>P</i> -value
Pen level			
Feedlot management			
Yearly placements	17 609 (2500, 62 000)	+0.000005	0.04
Use same pens for receiving and shipping	78% (96)	+0.25	0.21
Veterinary use	Veterinarian on staff 4% (5)	Referent	
	Private veterinarian regular visits 46% (56)	+0.77	0.02
	Private veterinarian as needed 50% (60)	+0.73	0.02
Cattle attributes			
Feedlot arrival — quarter of year	First guarter (Jan–Mar)	Referent	
(no placements in second quarter)	Third quarter (July-Sept)	-1.3	0.001
	Fourth quarter (Oct–Dec)	+0.77	0.001
Number of cattle in pen	144 (72, 283)	-0.004	0.00
Pen density (square feet/animal)	238 (107, 469)	-0.002	0.00
Cattle entry weight	737 (563, 883)	-0.006	0.00
Average miles transported	180 (12, 900)	+0.0009	0.00
Mass treated (metaphylaxis of all cattle in the pen	7% (9)	+0.9	0.00
with antibiotics to prevent respiratory disease)			
Cattle sex	Steers 60% (74)	Referent	
	Heifers 30% (37)	+0.9	0.00
	Mixed groups 10% (12)	+1.8	0.00
Cattle from multiple origins	14% (17)	+0.4	0.02
Cattle preconditioned	31% (38)	+0.18	0.2
Treated for internal parasites	87% (107)	+0.14	0.12
Treated for external parasites	80% (98)	+0.21	0.004
Week on feed $(1-12)^{r}$		-0.27	0.00
Vaccination practices			
Received initial vaccine on arrival (within 3 d)	78% (95)	+0.89	0.01
Received initial vaccine (within 3 d) of any type by agent	/ 0/0 ()))	10.09	0.01
BVDV	68% (83)	$\pm 0.61$	0.09
IBRV	75% (92)	+0.92	0.01
BRSV	56% (68)	+0.62	0.04
PLV	58% (71)	+0.50	0.10
Pasteurella (Mannheimia) haemolytica	22% (27)	+0.65	0.02
Haemophilus somnus	26% (32)	+0.04	0.89
$\mathbf{D}_{\mathbf{r}}$			
Received initial killed vaccine (within 5 d):	1/0/ (17)	10.72	0.02
	14%(1/) 100((12))	+0.73	0.03
	10% (12)	+0./2	0.10
	8% (10)	+0.99	0.01
$P_{3}^{1}$	10% (12)	+0.00	0.11
Harmothilus commu	100% (12)	+0.00	0.03
Themopritus somnus	10% (12)	-0.02	0.93
Received initial modified live vaccine (within 3 d)			
BVDV	55% (67)	+0.03	0.92
IBRV	65% (79)	-0.02	0.95
BRSV	48% (59)	+0.14	0.66
$PI_3V$	48% (59)	-0.09	0.77
Pasteurella (Mannheimia) haemolytica	15% (18)	+0.47	0.13
Haemophilus somnus	1/% (21)	-0.004	0.99
Revaccinated with any vaccine	33% (39)	+1.1	0.00

BVDV — Bovine viral diarrhea virus; IBRV — Infectious bovine rhinotracheitis virus; BRSV — Bovine respiratory syncytial virus; PI<sub>3</sub>V — Parainfluenza 3 virus

less potential bias than that of morbidity, so, in these data, it is possible that a perception by feedlot personnel of increased risk in long-haul cattle may have led to increased treatment rates. Alternatively, other differences between the studies may also be relevant. This study included both comingled and single source cattle, as well as auction market derived cattle, farm direct cattle, and cattle arriving from smaller feedlots for final finishing, and this different mix of risk factors may have allowed us to identify a relationship that was not apparent in the Canadian data, where other common risk factors may have overwhelmed any effect of transport. Additionally, transport distances in these data included pens of calves hauled from 0 km to 2833 km (0 to 1700 miles), allowing a broader range of potential risks. If transport distance is indeed a risk for increased morbidity, long-haul calves may need to be discounted or be the target of increased management interventions to control the morbidity risk. Alternatively short-haul calves may be worth a premium for the decreased risk of respiratory disease. These data indicate a 10% increase in initial respiratory disease morbidity risk for each 160 km (100 miles) increase in transport distance.

In this study, pens that contained mixed groups of steers and heifers were at increased risk for respiratory morbidity compared

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**Table 2.** Model associations with incidence of initial respiratory morbidiy counts, in

 122 pens of cattle on 102 feedlots

Variable	IRR	SEª	$P^{\mathrm{b}}$	95% CI
Gender category				
Steers	Referent			
Heifers	1.3	0.3	0.28	0.8, 2.0
Mixed heifers and steers	3.7	1.25	0.00	1.9, 7.2
Multiple sources (Y/N)	2.0	0.51	.008	1.2, 3.3
Pen average miles transported	1.001	0.0003	0.001	1.0004, 1.002
Entry weight < 250 kg (550 lb) 250–318 kg (550–700 lb)	Referent 0.52	0.2	0.09	0.25, 1.1
> 318 kg (700 lb)	0.18	0.07	0.00	0.08, 0.38
Weeks on feed				
Weeks 1–3	Referent			
Weeks 4–7	0.44	0.08	0.00	0.31, 0.61
Weeks 8–12	0.13	0.03	0.00	0.09, 0.19

<sup>a</sup> Semi-Robust Huber/White sandwich estimated standard errors

<sup>b</sup> Wald Chi-square statistics Dispersion 1.05

with pens that contained only steers or heifers. Other available studies have not reported this finding, but they have reported differences in respiratory morbidity or mortality risk between pens of heifers and pens of steers. Alexander et al (8), utilizing records from 17 696 cattle in a single feedlot, showed an increased incidence of lower respiratory tract disease in steers compared with heifers for the first 18 d on feed. Snowder et al (9) also reported increased respiratory morbidity in steers compared with heifers in a study involving 18 112 calves in 1 feedlot over 15 y. In contrast, a study of trends in mortality in 121 United States' feedlots showed an increase in respiratory mortality in heifers compared with steers during the period 1997 to 1999 (10). None of these studies reported on mixed groups of cattle. Ribble et al (11) found that steer calves arriving in groups too small to completely fill a truck were at increased risk for respiratory mortality. They hypothesized that this was due to their having mixed with other classes of cattle (heifer calves, or steer or heifer yearlings) in order to fill the truck. In the study reported here, only 10% of the pens of cattle were fed as mixed groups. Doing so may be a relatively uncommon management practice, but based on data from this analysis, it should be avoided when possible.

Pens containing cattle that originated from multiple different sources were also at increased risk for respiratory morbidity, presumably due to increased exposure and or stress. Mixing of cattle during procurement is a common practice in beef marketing. Mixing of cattle may increase stress by the interaction with new animals and the stress of establishing a social hierarchy. Additionally, mixing of cattle provides opportunity for the exposure of naïve animals to infected animals and the subsequent initiation of an outbreak. A similar relationship has been reported between level of pretransit mixing and mortality in other studies. In 1 report where most cattle were mixed at auction markets, the degree of mixing was associated with mortality risk from fibrinous pneumonia among different order buyers (11). In these data, cattle that arrived in a single shipment from an auction market or order buyer may have been classified as from a single source, even though they may have originated from multiple sources at purchase. This potential misclassification could have resulted in an underestimate of the effect of multiple sources on respiratory disease morbidity rate. The data reported here indicate that calves that are put together from multiple sources are twice as likely to suffer an initial respiratory morbidity during the first 12 wk on feed. This may be helpful in pricing and making management decisions for these calves.

Initial weight at entry to the feedlot was associated with morbidity incidence in these data. A greater incidence of respiratory disease is to be expected in calves compared with yearlings (12). Weight is likely an indicator variable for age in its relationship to morbidity risk. Young, lighter weight cattle are likely to be more naïve, having had less opportunity for exposure to potential pathogens over time and so having less immunity. Younger cattle may also experience more stress in the transition to the feedlot and may respond less efficiently and fully to exposure to respiratory pathogens compared to older cattle. While feeding calves is common in the North American feedlot industry, this analysis demonstrates that feedlots should expect increased morbidity due to respiratory disease.

Vaccination practices used by the feedlots in this study did not have any apparent effect on morbidity rate. Most pens of cattle were vaccinated with a modified live vaccine against viral respiratory pathogens on arrival. The limited number of pens that did not receive vaccination may not have provided adequate power to detect any effect on morbidity. The data did not include any information on specific brand of vaccines used. While vaccination of incoming feedlot cattle against respiratory disease is commonly practiced, little clinical trial data are available to support the use of respiratory vaccines in cattle (13). We also did not detect any effect of revaccination on respiratory disease morbidity rate. If revaccination was done as a management decision in response to high morbidity in a pen, we might have expected to see a positive association between revaccination and increased morbidity. Alternatively, if it was an efficacious practice regardless of pen morbidity status, we might have observed

a protective relationship. A lack of any relationship may indicate that revaccination is a feedlot management decision that is not made in response to individual pen morbidity.

We did not observe any relationship between prearrival processing of cattle and morbidity rate. In these data, cattle in 32% of pens were reported to have been processed prior to arrival, cattle in 49% of pens had not been processed, and in 19% of pens, the feedlot reported they did not know the preconditioning status of the cattle. Other data have supported the value of preconditioning calves prior to arrival at the feedlot when a period of holding postvaccination and weaning is observed (14,15). These data do not differentiate between different prearrival processing protocols, including whether any holding period was observed.

The proportion of feedlots returning pen morbidity data was modest (37.1% of 2nd phase participants). According to 1999 USDA:NASS cattle on feed data (16) of feedlots with capacity to hold greater than 1000 head at a single time, 76% held 1000 to 7999 head, and 24% held 8000 head or more. Large feedlots were overrepresented in the study reported here where 56% of feedlots returning data had a one-time capacity of 8000 head of cattle or more, so these data may be more of a reflection of the management practices and risks of larger feedlots. However, the feedlots reported here are similar in many respects to feedlots representing a broader national picture in the Unites States. Estimates of the United States' population from the Feedlot '99 survey indicate that 57% of placed cattle were steers (60% in this study) and 41% were heifers (30% in this study), but they did not provide data on mixed groups (17). The Feedlot '99 survey reported 82% of feedlots processed cattle within 3 d of arrival (78% in this study), and that 97.8% of cattle received an initial vaccination for respiratory disease on arrival (99% in this study). However, feedlots with onetime capacity of 8000 head or more in the Feedlot '99 survey reported a higher percentage of cattle with BRD than feedlots with less than 8000 head (15.5% versus 8.7%) (4). The larger lots in this study may have represented a higher treatment rate than the national average; however, the percentage treated for BRD in this study (5.9%) was lower than that of the Feedlot '99 national estimate for either feedlot size.

One weakness of the current study is the lack of a consistent, validated case definition for respiratory disease. This is a common problem for many large scale observational studies and could result in differential bias if differing case definitions between feedlots are also related to specific management practices. The data available in this study do not allow an evaluation of this potential bias. Clearly one would expect some level of difference between feedlots in the definition of respiratory morbidity; however, there is a relatively common understanding within the feedlot industry regarding the identification of respiratory morbidity that includes depression, elevated rate of or difficulty in respiration, and elevated temperature. Still the data reported here are based on perceived morbidity and are a direct measure of treatment risk rather than morbidity. This is a common issue for all feedlot morbidity data. Results of this analysis suggest important factors that increase risk for respiratory morbidity. In some cases, avoidance of these risks may be prudent for the feedyard in order to control morbidity risk. In many cases, some or all of these practices cannot be avoided. These data may be useful to better understand the increase in respiratory morbidity likely to occur, but they are also biased toward larger feedlot sizes. With this information better decisions can be made to assure that adequate labor is available to manage increased morbidity and that the purchase price is adjusted to account for the increased morbidity.

## Author contributions

Each author was involved with all phases of the project from study design to analysis and manuscript preparation.

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