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PRODUCTION AND MANAGEMENT: *Original Research*

Determining relevant risk factors associated with mid- and late-feeding-stage bovine respiratory disease morbidity in cohorts of beef feedlot cattle

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ABSTRACT

Objective: Previous bovine respiratory disease (BRD) research has focused on events early in the feeding phase, but the objective of this study was to determine characteristics and risk factors associated with cohort-level BRD morbidity in the middle and late portions of the feeding phase.

Materials and Methods: The analysis was performed on records from 13 commercial feedlots in the United States from 2017 through 2020. Cohorts were analyzed over their first 100 d on feed. Two methods of classification were used. In the veterinarian classification method, hierarchical clustering created 20 temporal patterns, which were categorized by veterinary consultants as early-feeding-stage, mid-feeding-stage, or late-feeding-stage morbidity curves. In the days classification method, cohorts were categorized based on which portion of the feeding period (0 to 42 d, 43 to 71 d, or 72 to 100 d) had the greatest percentage of treatments for BRD. An events/trials model was used to determine morbidity and mortality across different stages of the feeding phase. Ordinal regression was used to determine associations between cohort characteristics and BRD timing. Year and feedlot were included as random effects to account for the hierarchical structure of the data.

Results and Discussion: Combined classification yielded 2,429 early-feeding-stage cohorts, 108 mid-feeding-stage cohorts, and 61 late-feeding-stage cohorts. The only factor significantly ($P < 0.05$) associated with cohort-level BRD morbidity timing was quarter of arrival. Cattle arriving in the second quarter (Q) were more likely to be mid-feeding stage or late-feeding stage (5.5%, 10.2%, respectively) compared with cattle arriving in the other quarters of the calendar year (Q1: 2.7%, 4.5%; Q3: 1.4%, 2.2%, or Q4: 1.4%, 2.3%).

Implications and Applications: This study evaluated risk factor relationships with cohort-level BRD timing. No cattle characteristics were significantly associated with BRD timing; however, cattle arriving in Q2 were at higher risk for cohort-level mid- or late-feeding-stage BRD.

Key words: bovine respiratory disease, late-feeding stage, morbidity, timing

INTRODUCTION

Bovine respiratory disease (**BRD**) has persisted as the leading cause of morbidity and mortality in North American feedlots, which also makes it known as the most economically impactful cause. Estimates have shown that 67 to 82% of total feedlot morbidity is due to BRD (Smith, 1998). Previous research has focused on BRD soon after arrival to the feedlot (Babcock et al., 2010; Vogel et al., 2015). Research between 1986 and 1994 indicates that approximately 65 to 80% of morbidity occurred before 45 d on feed (**DOF**), 13 to 22% from 45 to 90 DOF, and 6 to 15% after 90 DOF (Edwards, 1996). There is a gap in the literature about the timing of BRD at the cohort or individual level, and the existing literature is over a decade old. Recent literature suggests a possible shift from the previously reported epidemiological pattern (Theurer et al., 2021). An attempt was made recently to determine differences in timing of BRD morbidity between high-risk and high-performing cattle cohorts throughout the feeding phase; however, no potential causes of BRD later in the feeding period were evaluated (Theurer et al., 2021). Due to a possible increase in incidence later in the feeding period, more research focused throughout the entirety of the feeding period is necessary. From an economic perspective, loses later in the feeding period are more detrimental as the cumulative resources expended are greater than a loss at the beginning of feeding.

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A major deficiency in the literature to date has been no definition for "late" feeding mortality (Engler et al., 2014), and late-feeding-stage morbidity suffers from similar issues. Without a clear case definition, determining potential influence of risk factors is challenging. The objective of this work was to determine cohort-level associations with the timing of BRD morbidity and to define a case definition for the timing of cohort-level BRD. A secondary object was to determine differences in amount of morbidity and mortality across different stages of the feeding phase.

MATERIALS AND METHODS

Data Source

Lot-level data from 13 feedlots were collected under confidentiality agreement with the individual feedlots. Institutional Animal Care and Use Committee (IACUC) approval was not required as historical operational data were used for the analysis. The Institutional Review Board at Kansas State University, application #10348, was deemed exempt from in-depth review and granted permission for use of a survey. All veterinarians that participated in the survey did so anonymously.

A "cohort" was defined to be a group of animals that arrived at the feedlot together; they did not have to finish out the entire time on feed in the same pen. Data were imported into RStudio (9) for analysis; there were 8,764 cohorts, each cohort containing at least one record for an animal treated for BRD. Records were from May 25, 2017, through June 17, 2020. Our case definition for "BRD" was any animal identified by feedlot personnel with clinical signs consistent with BRD for the first time in the feeding period and subsequently treated with an antimicrobial by feedlot personnel. Animals were not excluded due to multiple treatments; however, only the first pull was considered for this analysis. Cohorts were limited to 30 and 500 animals at arrival, greater than 7% total BRD morbidity, single-sex cohorts, and an average arrival weight between 181 kg (400 lb) and 454 kg (1,000 lb). There were 3,550 cohorts that met these initial criteria (Figure 1).

Data were transformed into a format in which every cohort had an observation for each individual day from 0 to 100, creating a data set for number of animals treated for BRD each day. This was done to create equal weight in the temporal patterns for each cohort as animals were fed to many different final days. Variables were calculated for the cumulative treatments out of the total treatments per cohort and of the treatments in a lot out of the total animals in that lot. Continuous variables were categorized based on biological cutoffs or quarters to avoid violating the linearity assumption (Table 1).

There is no previously published case definition of early-feeding-stage, mid-feeding-stage, and late-feeding-stage timing for cohort BRD morbidity; therefore, we decided to combine 2 categorization methods to classify the timing of BRD, the first of which used hierarchical clustering based on cumulative BRD morbidity to create daily incidence curves and asking consultant veterinarians to classify each curve as having a pattern consistent with early-feeding-stage, mid-feeding-stage, or late-feeding-stage BRD. The second approach was to categorize cohorts based on which feeding period (early-feeding stage, mid-feeding stage, or late-feeding stage) had the greatest percentage of BRD morbidity. Combining 2 classification methods was done to increase specificity of our case definition so that any cohort classified as having late-feeding-stage BRD would likely receive that classification by a strong majority of feedlot veterinarians.

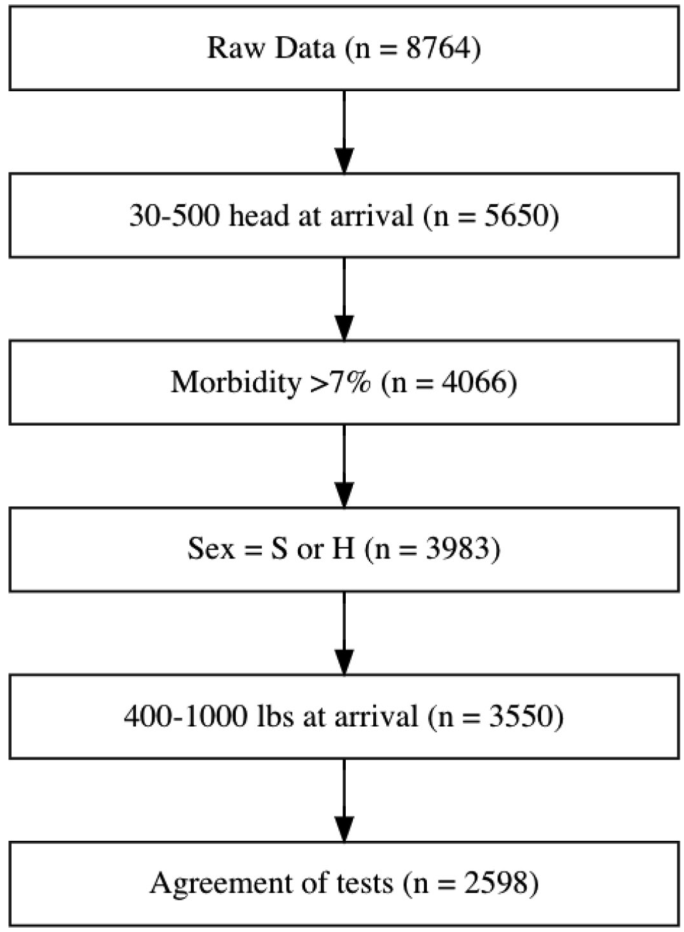

Figure 1. Flowchart describing the inclusion criteria for 13 feedlots into the working data set. All numbers are representative of number of cohorts. S = steer; H = heifer; 400–1,000 lbs = 181–454 kg.

Veterinary Consultant Survey Classification

In the first classification, clusters of BRD incidence curves were created using Ward's method, which is an agglomerative clustering technique that minimizes sum-of-squares (Ward, 1963). Agglomerative clustering is a type of clustering that starts with each individual observation and works forward grouping them to a specified cut point. Twenty clusters were formed using a process where a cut point was chosen when an adequate number of cohorts

Table 1. Variables used in the working data set

Variable	Description
Headin	Number of animals in the cohort at arrival
Sex	Steer or heifer
QuarterArrival	Quarter of arrival at the feedlot (1: January–March, 2: April–June, 3: July–September, 4: October–December)
Time	Bovine respiratory disease incidence curve category (early-feeding stage, mid-feeding stage, late-feeding stage)
NumberTrt	Total number treated from d 0–100 per cohort
DOF	Count of days on feed from d 0–100 per cohort
NumberTrtPerDay	Count of number treated from d 0–100 per cohort
Total100dTrt	Total treatments in the cohort from d 0–100
CumsumPercent	Cumulative number treated by day/total treated
CumsumCohort	Cumulative number treated by day/total animals in the cohort at arrival
Yardlot	Unique identifier for each cohort

remained in each cluster and merging groups one more time showed an evident loss of information. Each cluster represented at least 46 cohorts, and clusters were graphed as percentage of treatments per day for visualization. The percentage of treatments per day curves for each of the 20 clusters were built into a survey on Qualtrics (2005; www.qualtrics.com), which was sent out as a convenience sample of consulting veterinarians. The survey asked each veterinarian to classify each plot as depicting early-feeding-stage, mid-feeding-stage, or late-feeding-stage cohort-level BRD morbidity timing (Figures 2–4).

Days Classification

In the second classification, method cohorts were categorized based on which feeding period had the greatest percentage of BRD cases. Feeding intervals were set as d 0 to 42, 43 to 71, and 72 to 100. Previous literature has stated that 75% of BRD morbidity occurs by d 42 on feed (Babcock et al., 2010), and for our purposes, this was defined as early-feeding stage. The mid-feeding-stage and late-feeding-stage categories were decided on by allotting half the remaining DOF to each category. Percentage

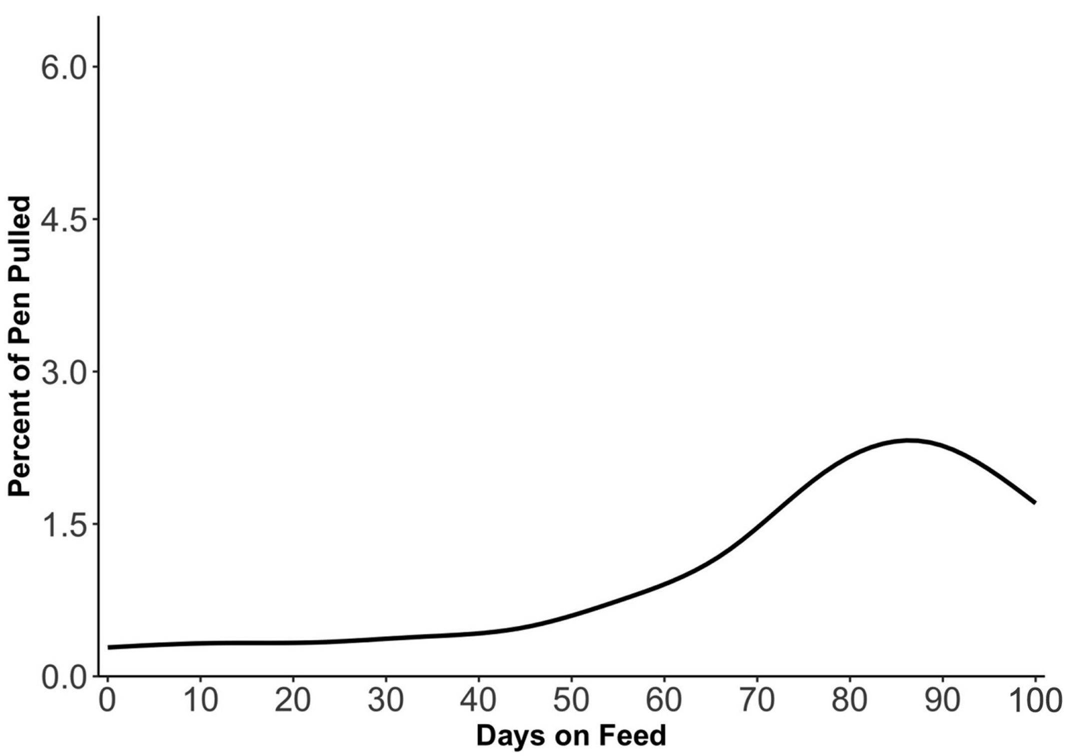

Figure 2. Example of 1 of the 20 clusters of incidence for the percentage of a pen pulled from 0 to 100 d on feed. This cluster represents 46 different cohorts and was determined to be late-feeding-stage morbidity by all veterinarians consulted.

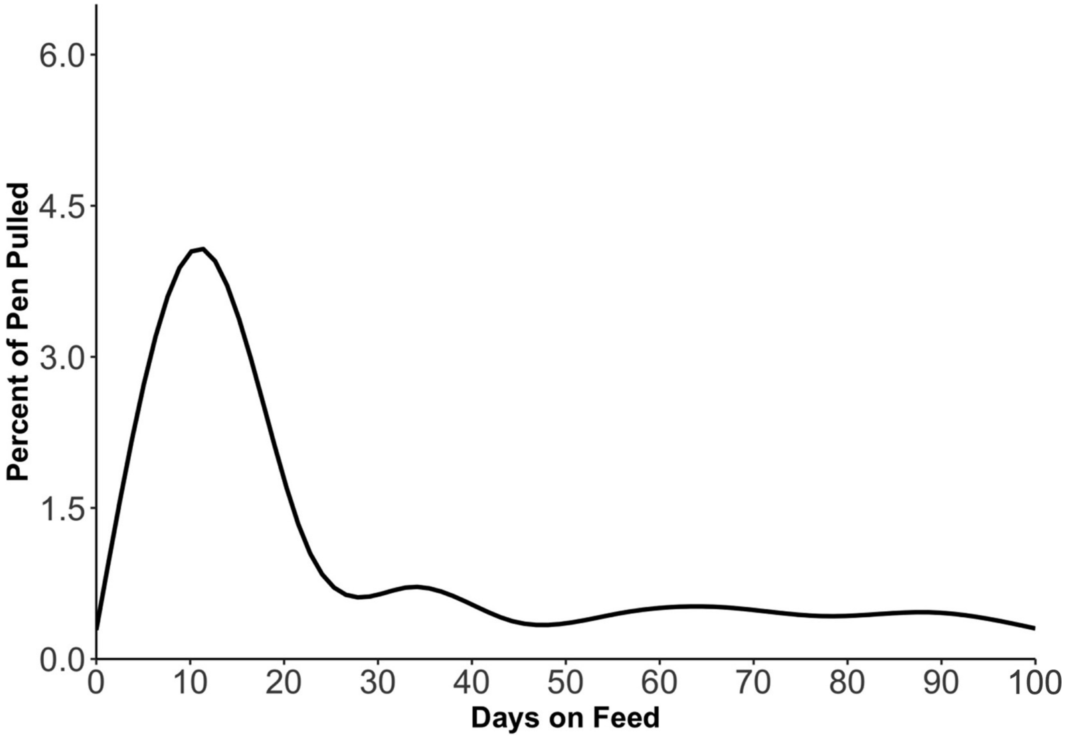

Figure 3. Example of 1 of the 20 clusters of incidence for the percentage of a pen pulled from 0 to 100 d on feed. This cluster represents 209 different cohorts and was determined to be early-feeding-stage morbidity by all veterinarians consulted.

of overall BRD morbidity within cohort was calculated for each interval, and whichever interval had the greatest number of treatments was assigned the classification. Agreement of classification methods was used to create a data set of cohorts that met our final case definition for the timing of cohort-level BRD morbidity.

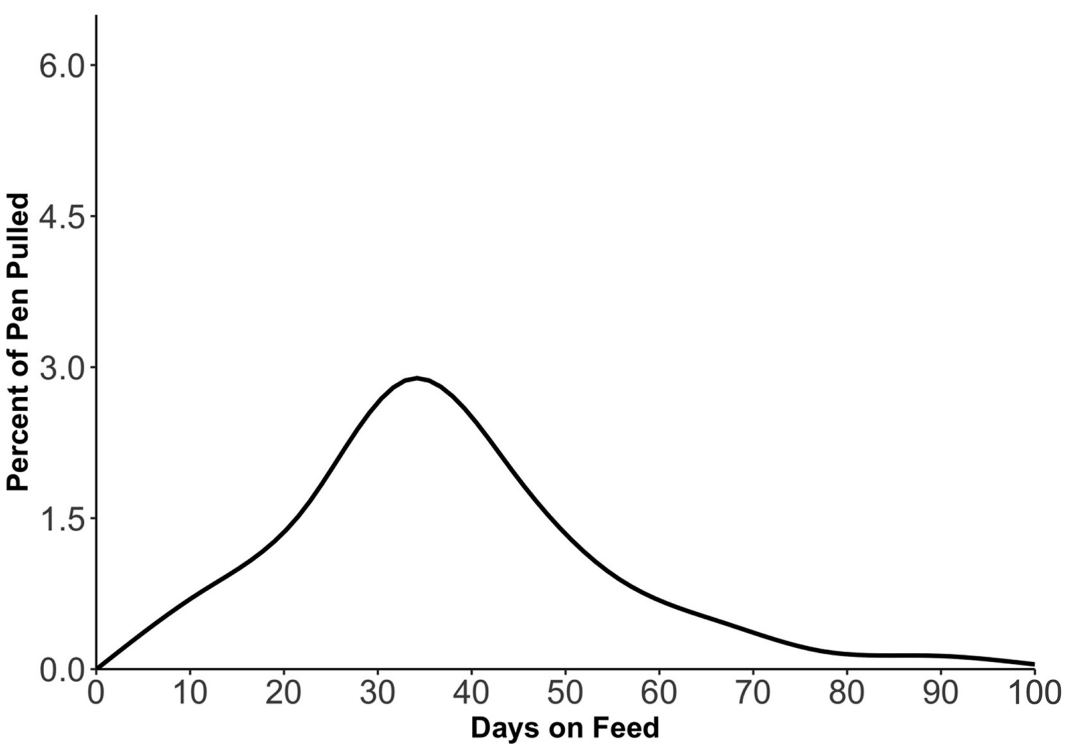

Figure 4. Example of 1 of the 20 clusters of incidence for the percentage of a pen pulled from 0 to 100 d on feed. This cluster represents 158 different cohorts and was determined to be mid-feeding-stage morbidity by all veterinarians consulted.

Statistical Analysis

An events-over-trials regression mixed-effects model was fit using the 'glmer' function from the 'lme4' package in RStudio (RStudio Team, n.d.). The outcome variable was the number of treatments or population at risk within cohort. "Population at risk" was defined by number of cattle in the cohort at arrival less number treated per day as defined previously (Cernicchiaro et al., 2012). The independent variable for this analysis was the ordinal variable "time," which had categories for early-feeding stage, mid-feeding stage, or late-feeding stage. Feedlot and year were included as random effects to account for the hierarchical nature of the data. A similar model was fit to identify differences in mortality for the independent variable "time" with random effects for feedlot and year. This model used outcome variable deaths(events)/population at risk (trials), with "population at risk" defined as number of cattle in the cohort at arrival less the number dead by day. The logistic regression model was fit to evaluate differences in morbidity and mortality across cohorts that were classified as early-feeding stage, mid-feeding stage, or late-feeding stage.

An ordinal regression mixed-effects model was fit using the 'clmm' function from the 'ordinal' package in RStudio (RStudio Team, n.d.) to analyze which cohort-level risk factors were associated with the outcome of interest (early-feeding-stage, mid-feeding-stage, or late-feeding-stage cohort BRD timing). Covariates evaluated for the model were sex, arrival quarter, in-weight category, lot size category at arrival, and all possible interactions. Random effects of feedlot and year were included to account for lack of independence of the feedlots and years. All potential interactions were evaluated using forward manual selection. Main effects variables were screened by backward elimination until only statistically significant ($P < 0.05$) variables remained for the final model. Probabilities were used to evaluate the predictor variable.

RESULTS AND DISCUSSION

Previous literature evaluated factors related to BRD at arrival and within the early weeks in the feedlot. Bovine respiratory disease morbidity is most predominant within the first 30 d for feedlot cattle in Brazil (Baptista et al., 2017), and a US study found that 74% of BRD cases occurred within the first 42 DOF (Babcock et al., 2009). Although a study recently investigated BRD at ≥45 DOF (Theurer et al., 2021), the current study helps fill in the gap of research specifically addressing factors associated with timing of disease through the first 100 DOF. Previously, there was no case definition of late-day cohort-level morbidity and no previous methodology to assign cohorts to a timing of disease category. Our case definition for cohort-level BRD timing was created based on agreement between a classification method that surveyed consultants to classify clusters of BRD incidence curves and classification based on which of 3 feeding periods had the greatest percentage of BRD cases for each cohort.

Classifying Cohorts Based on the Timing of BRD Morbidity

Thirteen surveys were returned and evaluated. Using the survey answers, the BRD timing classifications for individual cohorts were defined based on the classification of each cluster by most the consultants. Using this method, there were 2,581 early-feeding-stage, 892 mid-feeding-stage, and 120 late-feeding-stage cohorts. Agreement among the consultants' cohort-level classification was at minimum 61.5% for each of the 20 clusters. There was at least one cluster from early-feeding stage, mid-feeding stage, and late-feeding stage that had 100% agreement among consultants, but more often than not, at least one consultant disagreed with the rest. Some possible explanations for disagreement among consultants would be that different consultants work with different populations of cattle and are accustomed to different disease patterns. Another explanation could be that some cluster graphs were not a clean-cut distribution of disease, in that some curves had 2 peaks and consultants were not provided a bimodal option. Based on the method of percentage BRD morbidity by interval, 3,280 cohorts were defined as early-feeding stage, 239 as mid-feeding stage, 74 were defined as late-feeding stage.

Combination of Both BRD Timing Classification Systems

Creating a data set of cohorts with perfect agreement when both classification methods were combined (n = 2,598) increased specificity of our case definition and resulted in 1,121 cohorts being removed due to disagreement among classification methods. The final, combined method data set contained 2,429 early-feeding-stage, 108 mid-feeding-stage, and 61 late-feeding-stage cohorts (Table 2). Of the cohorts removed, the greatest loss was where the days classification method classified the cohort as being early-feeding stage, but the consultant survey method classified them as mid-feeding stage.

Results from the logistic regression events-over-trials morbidity model showed a greater incidence of morbidity in the early-feeding-stage category (16.08%) compared with mid-feeding-stage (14.31%) or late-feeding-stage (12.23%) categories. The logistic regression events-over-trials mortality model identified the greatest mortality in early-feeding-stage cohorts (2.97%) compared with mid-feeding-stage (2.48%) or late-feeding-stage (2.55%) cohorts.

No interactions were found significant at the $P < 0.05$ level, and therefore, all were excluded from the model. The only variable significantly ($P < 0.01$) associated with timing of BRD at the pen level in this study was quarter of arrival into the feedlot. The percentage of cohorts that arrived in the first, second, third, or fourth quarter that

Table 2. Descriptive demographics of cohorts by timing category

	Time		
Variable	**Early**	**Mid**	**Late**
Quarter of arrival			
1	620	34	19
2	292	33	19
3	567	17	6
4	950	24	17
Sex			
Steer	1794	67	38
Heifer	635	41	23
Cohort size			
30–100	529	42	18
101–150	583	21	20
151–200	596	20	9
201–300	526	20	12
301–500	194	5	2
Average weight at arrival (kg)			
181–226	53	3	2
227–272	196	11	7
273–318	638	30	16
319–363	753	30	18
364–409	560	24	13
410–455	229	10	5

Table 3. Model estimated probabilities and standard error of BRD morbidity by quarter of arrival

Time and quarter of arrival	Probability (%)	SE
Early-feeding stage		
1	92.5[a]	0.019
2	84.2[b]	0.039
3	96.4[a]	0.011
4	96.3[a]	0.011
Mid-feeding stage		
1	2.8[a]	0.007
2	5.5[b]	0.014
3	1.4[a]	0.004
4	1.4[a]	0.004
Late-feeding stage		
1	4.7[a]	0.013
2	10.3[b]	0.028
3	2.2[a]	0.007
4	2.3[a]	0.007

[a,b]Different superscripts within a category indicate statistically significant differences ($P < 0.05$).

were classified as having early-feeding-stage BRD were 92.9, 84.3, 96.4, and 96.2%, respectively. Cohorts arriving in the second quarter had a 5.5% probability of being classified as having mid-feeding-stage BRD, which was significantly different compared with 2.7, 1.4, and 1.4% for cohorts arriving in the first, third, or fourth quarters (respectively). Cohorts arriving in the second quarter had a 10.2% probability of being classified as having late-feeding-stage BRD, which was significantly different compared with 4.5, 2.2, and 2.3% for the cohorts arriving in the first, third, and fourth quarters (respectively). Cattle cohorts were most likely to be either mid-feeding stage or late-feeding stage when BRD morbidity occurred if they arrived in the second quarter (April to June; Table 3). Out of all the quarters, the second quarter represented the lowest percentage (14%) of animals arriving at the feedlot. Possible explanations for quarter of arrival being associated with BRD morbidity is that the type of cattle arriving in the second quarter may have some differences compared with those arriving the rest of the year. Some of these differences could be that the cattle market and production cycle dictate a large influx of predominantly high-risk animals arrive in the feedlot in the fall (Ribble et al., 1995; Taylor et al., 2010; Babcock et al., 2013). Commonly, cattle are spring born and either shipped to the feedlot in the fall immediately after weaning or retained and backgrounded for a short 30- to 60-d program or longer 90- to 120-d program (Taylor et al., 2010).

This analysis was performed on cohort-level data to identify factors associated with timing. It is not surprising to the authors that factors known to be associated with the incidence of BRD in the feedlot were not significantly associated with the timing of BRD. Further research is necessary to identify risk factors associated with mid-feeding-stage and late-feeding-stage BRD morbidity and mortality at the individual animal level. We recognize that the BRD morbidity reported in this study is greater than reality due to the inclusion criteria of >7% BRD morbidity per cohort. Across the United States in 2011, NAHMS stated that 13.4% of cattle placed in a feedlot were treated with an antimicrobial for BRD, so the cut point used here is still well below the average morbidity across feedlots (NAHMS, 2011). Additionally, there was an imbalance of cohorts in the timing categories, with the fewest cohorts being considered late. Due to the total number of cohorts involved in this study and statistical tests used, this is not of major concern but should be noted as potential associations could have been missed because of the smaller number of cohorts. In addition, interpretation of observational studies of feedlot data must recognize that different personnel are identifying sick calves with different diagnostic protocols in place at each feedlot. Potential confounding factors need to be considered when interpreting the results of this study; some examples of this would be differences in management between feedlots, biological differences between animals, background, and previous management of animals. Our analysis was done to account for sources of variability that we know have an effect on our outcome by including feedlot and year as random effects in the model.

APPLICATIONS

Evaluating the timing of BRD morbidity in the feedlot illustrated a significance of the quarter of arrival, with the greatest amount of late-feeding-stage BRD occurring in cattle that arrived between April and June. Further investigation into why animals arriving in the second quarter of the year have greater risk for late-feeding-stage BRD morbidity needs to be done. Our data represented 13 feedlots from the central United States, so caution needs to be taken when interpreting these results to feedlots in other geographic locations and with other management practices.

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