Risk factors associated with case fatality and treatment success following initial bovine respiratory disease treatment in feedyard cattle

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Abstract

Bovine respiratory disease (BRD) is an important disease of fed cattle and knowledge gaps exist regarding factors predicting treatment success. The study objective was to identify potential relationships between risk factors known at the time of initial BRD treatment with 3 post-treatment outcomes: first treatment success (FTS; finishing feeding phase with no further treatments for any disease), non-cause specific case fatality risk (CFRALL; post-treatment deaths from any cause), and cause-specific case fatality risk (CFRBRD; deaths attributed to BRD). This retrospective analysis used generalized linear mixed models to evaluate relationships between covariates of interest (arrival: sex, weight, month; treatment event: days on feed (DOF), rectal temperature, day-of-week, antibiotic drug class) with each outcome (FTS, CFRALL, CFRBRD). Analysis included 132,521 individual-animal initial BRD treatment records from 14 central U.S. feedyards (May 2017 to Dec 2020) with overall FTS of 67.8%, CFRALL of 10.0%, and CFRBRD of 6.3%. The FTS was associated ($P < 0.05$) with all covariates except sex, CFRALL was associated with all covariates, and CFRBRD was associated with all covariates except day-of-week treated. Treatments early in the feeding phase (DOF 0-10, 11-20) resulted in lower ($P < 0.05$) FTS (49.2% ± 0.8; 55.3% ± 0.8), higher ($P < 0.05$) CFRALL (12.5% ± 1.3; 12.6% ± 1.4) and higher ($P < 0.05$) CFRBRD (6.3% ± 1.1; 6.1% ± 1.0) compared to cattle treated on days 21-70. Rectal temperature in the 103.1-104.0 (39.4-40.0 °C) category had higher ($P < 0.05$) CFRALL (15.3% ± 1.5) and CFRBRD (9.2% ± 1.5) compared to other rectal temperature categories. Specific risk factors including days on feed at treatment, sex and weight at the time of treatment were associated with treatment outcomes. Results can be useful for defining expectations following first treatment for BRD.

Key words: bovine respiratory disease, case fatality risk, first treatment success, risk factors, antimicrobials

Introduction

Bovine respiratory disease (BRD) remains a significant challenge for the beef industry. The syndrome is common, with approximately 97% of feedyards administering antimicrobial treatments to cattle affected with BRD[1] resulting in significant economic cost to the beef industry.[2,3] Welfare and financial impacts of BRD emphasize the importance of designing and managing appropriate therapeutic interventions. Multiple studies have evaluated factors associated with BRD morbidity and mortality risk,[4–7] and economic impacts;[8–10] however, few studies have focused on identifying factors associated with post-BRD treatment success or failure.

Common post-treatment evaluation metrics are case fatality risk and first treatment success. Several variables influence the likelihood of treatment success, and improved understanding of potential causes of treatment failures facilitates refining therapeutic protocols.[11] Previous studies have evaluated physiological (e.g., rectal temperature) or pathological (e.g., blood metabolites) parameters associated with BRD case outcomes.[12–16] Cattle demographic factors (e.g., sex, arrival weight) have been infrequently evaluated combined with information known at initial treatment (e.g. days on feed (DOF), rectal temperature, and selected antimicrobial) when evaluating differences in case outcomes. Avra et al. evaluated initial BRD treatment success and determined arrival factors including risk classification, DOF, quarter of arrival, and rectal temperature were associated with the likelihood of treatment failure; however, potential differences between treatment failure resulting in retreatment versus death were not elucidated.[17] Theurer et al. evaluated the likelihood of cattle not finishing the feeding phase, but no evaluation of retreatments were performed.[14] Identifying risk factors associated with treatment success as gauged by retreatment or cause-specific mortality allows feedyard personnel to better anticipate likely outcomes following initial treatment for BRD.

The objective of this retrospective analysis was to identify potential association between risk factors known at the time of first BRD treatment with 3 post-treatment outcomes: first treatment success, (FTS; percent of animals requiring no further treatment and finishing the feeding phase), non-cause specific case fatality risk (CFRALL; mortalities following treatment from any cause), and cause-specific case fatality risk (CFRBRD; mortalities attributed to BRD).

Materials and methods

This retrospective analysis used existing feedyard operational data and was exempt from Institutional Animal Care and Use Committee approval as no animals were used specifically for this study. The project included data from 14 commercial U.S. feedyards from May 31, 2017 through December 28, 2020. Included feedyards were located in the U.S. central High Plains region. Data were included from native (beef) as well as dairy-influenced or mixed breeds of cattle. However, breed of animal was not available in the records to be included in the statistical analyses as a potential risk factor.

Data management

The initial dataset contained data for individual-animals (n = 269,683) at the time of first treatment for any disease. Observations were filtered to meet ensuing inclusion criteria. Metaphylactic status was not included in this analysis as it was not known for all feedyards. Only cattle with a clinical diagnosis of BRD at first treatment that received an antimicrobial were included. The BRD diagnosis was performed by personnel at each feedyard. Diagnostic criteria varied slightly between feedyards, but included clinical signs consistent with respiratory disease, namely depression, anorexia and increased respiratory rate/effort. Average cohort arrival weight was limited to cohorts between 500-1100 lbs. (226.8-499 kg) and only cohorts with sex described as either steer or heifer were included (excluding mixed sex and non-labeled cohorts). Cohort size was restricted to ≤ 400 with no minimum number of animals received per group. The days on feed (DOF) at the initial BRD treatment event was limited to between 0 and 300 days. Finally, rectal temperature at the time of initial BRD treatment was limited to between 100.4 and 109.4°F (38 and 43°C) to minimize potential temperature recording errors.

After filtering, data were imported into statistical software[a] for management and analysis. Continuous variables were categorized to avoid violation of assumption of linear associations with outcomes of interest. Arrival dates were categorized to represent the month cattle entered the feedyard. Arrival weight categories were assigned in 100 lb. (45 kg) increments to represent weight ranges commonly used in cattle sales transactions (500-599, 600-699, 700-799, 800-899, 900-999, 1000-1100 lb.; 227-272, 273-317, 318-362, 363-407, 408-452, 453-497 kg). Categories for DOF at initial treatment ranged from 0 to 100 days in 10-day increments, with a single additional group for > 100 days. Recorded treatment dates were categorized by day of the week at the time of treatment. Rectal temperature measurements were categorized based on measurements as recorded in °F and converted to °C. The categorization was based on rectal temperatures less than or equal to 103, 103.1-104.0, 104.1-105, 105.1-106, and greater than 106 °F. This resulted in categories in °C of < 39.4, 39.4 – 40.0, 40.1-40.6, 40.7 – 41.1, and > 41.1 °C. Antimicrobial treatment for the first BRD diagnosis was classified by antimicrobial types into beta lactams, fluoroquinolones, macrolides, phenicols and tetracyclines.

Risk factors known at the time of initial BRD treatment fall into 2 broad categories: arrival cohort-level information and individual-animal treatment event data. Arrival information includes sex, arrival month, and cohort average arrival weight. Individual-animal information at initial BRD treatment event includes the DOF at treatment, rectal temperature, day-of-week treatment occurred, and antibiotic drug class used.

Outcomes of interest

Measured outcomes were first treatment success, mortality risk (CFRALL; deaths from any cause following treatment), and cause-specific case fatality risk (CFRBRD; deaths attributed to BRD). The FTS was calculated as animals treated for the first time for BRD that received no subsequent treatments for BRD and finished the feeding phase divided by total animals initially treated for BRD with no subsequent treatments for BRD. All cause case fatality risk (CFRALL) was calculated as animals treated for BRD only once that later died of any cause divided by all animals initially treated for BRD only once. The BRD specific case fatality risk definition (CFRBRD) was calculated as animals initially treated for BRD and died with a mortality diagnosis of BRD (as defined by the feedyard personnel via necropsy), divided by all animals initially treated for BRD. Morbidity and mortality diagnoses for individual animals were made at the feedyard level by trained personnel.

Statistical analysis

Statistical models were created using generalized linear mixed models[a] using the glmer function. Separate models were created for each outcome (FTS, CFRALL, CFRBRD) to evaluate potential associations with study factors of interest including arrival factors (sex, average cohort weight category, arrival month) and initial treatment event factors (DOF at treatment, rectal temperature category, day-of-week treated, and antibiotic class). Random effects for each cohort nested within feedyard and arrival year were incorporated in each model to account for the lack of independence for cattle from the same cohort and feedyard. Multivariable models were constructed through a backward iterative process until only variables significantly ($P \leq 0.05$) associated with the outcome remained in each model. Potential differences among model least squares mean probabilities among levels of each covariate were evaluated and adjusted for multiple comparisons using Tukey HSD with $P \leq 0.05$ considered significant.

Results

Initial data consisted of individual-animal treatment records (n = 269,683) for cattle treated for all causes. After filtering criteria (Figure 1) were applied, 132,521 individual-animal initial BRD treatment records were available for analysis. Overall FTS in the final dataset was 67.8% (89,885/132,521) with CFRALL of 10.0% (13,248/132,527) and CFRBRD of 6.3% (8,414/132,521).

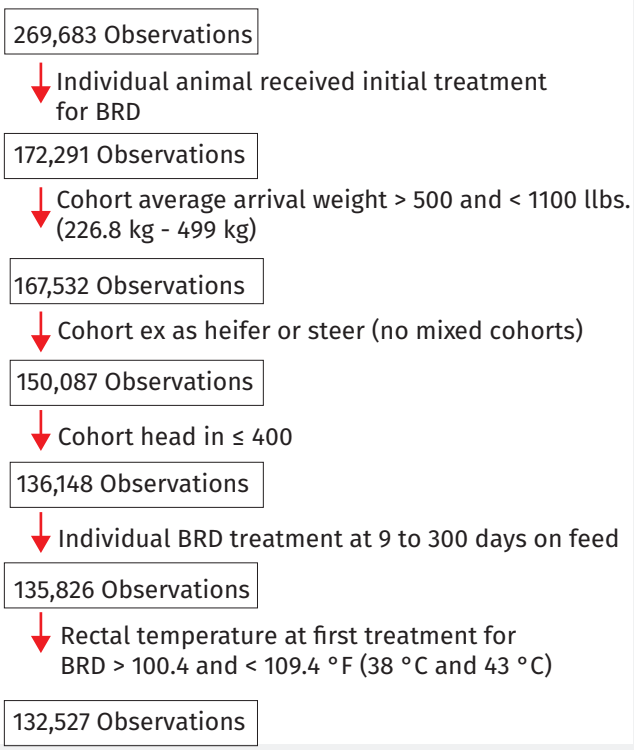
The study population consisted of 74.3% steers with 81.8% of the study population arriving with average cohort arrival weight between 700 and 1,000 lbs. (317.6 and 453.6 kg). Study animals arrived throughout the year with 43.3% of the arrivals between September and December. Most BRD treatment events occurred early in the feeding phase with 73.3% of initial treatments prior to 50 DOF. The majority (68.9%) of rectal temperatures were above 104.0 °F (40.0 °C) at the time of initial treatment. Cattle were initially treated for BRD at similar frequency on each day-of-week with the percent of BRD treatments ranging from 13.1% to 15.1% of all treatments occurring on each day. Macrolides were the most common (68.0%) antimicrobial class at first treatment. Descriptive statistics by each potential risk classification variable are provided in Table 1.

First treatment success (FTS)

The final multivariable model for FTS included significant associations ($P \leq 0.05$) with arrival (cohort average weight category, month), and initial treatment factors (DOF at treatment, rectal temperature, day-of-week and antimicrobial class). Arrival year was not able to be included in the model due to a lack of convergence. Cohort sex was not ($P = 0.13$) associated with FTS. Model-adjusted probabilities for each covariate are displayed in Table 2.

Cattle with average cohort arrival weight of 600-699 lbs. (272.3-317.5 kg) had the lowest ($P \leq 0.05$) probability of FTS (53.5% ± 1.2) compared to all other weight classes. Each subsequent weight class had higher ($P \leq 0.05$) probability of success through the

Figure 1: Data filtering on initial treatments at feedyards U.S. central high plains (n = 14) to create dataset consisting of individual animal initial treatments for bovine respiratory disease (BRD) based on inclusion criteria.



1,000-1,100 lb. (453.7-499.0 kg) category (66.0% ± 0.8). The lowest weight class (226.8-272.2) did not differ ($P > 0.05$) from the highest 2 weight classes in the model-adjusted likelihood of FTS. Cattle arriving in September (66.2% ± 0.8) did not differ from cattle arriving in October, but had higher FTS compared to all other arrival months. Cattle treated at early DOF (0-10: 49.2% ± 0.8; 11-20: 55.3% ± 0.8) or late in the period (> 100: 54.0% ± 0.9) had lower FTS compared to all other categories. Cattle with rectal temperatures below 103 °F (39.4 °C) had the best first treatment success (66.3% ± 0.7) compared to all other categories. While day-of-week at initial treatment was statistically associated with FTS, few clinically meaningful differences were identified. Cattle initially treated with antibiotics from macrolide or tetracycline classes had higher FTS (69.9% ± 0.4; 69.1% ± 0.4, respectively) compared to other antibiotic classes, but did not significantly differ from each other.

Case fatality risk all

The non-cause specific post-treatment mortality model revealed all arrival and initial BRD treatment event factors were significantly ($P \leq 0.01$) associated with CFRALL and model estimates for each level of the covariates are included in Table 2. Arrival year was not able to be included in the model due to a lack of convergence. Heifers had higher CFRALL (11.8% ± 1.2) compared to steers (10.3% ± 1.0). Few differences were identified based on arrival average cohort weight category; however, cattle in the 800-899 lbs. (363.0-408.2 kg) category had higher CFRALL (11.7 ± 1.2) compared to cattle in the 1000-1099 lbs. (453.7-499.0 kg) category (10.0 ± 1.1). Cattle arriving in January and February had higher CFRALL compared to cattle arriving in August, September and October, and the remaining months did not differ from either of these periods. Cattle treated at > 100 DOF had the overall highest CFRALL (19.1% ± 1.2); however, cattle treated in the first 30 DOF had higher CFRALL compared to cattle treated d 31-50. Cattle treated on Sundays had higher CFRALL (11.7% ± 1.2) compared to cattle treated on Fridays (10.3 ± 1.1), but neither day differed from any other day of the week. Cattle treated with tetracyclines had a lower CFRALL (7.7% ± 0.8) compared to most drug classes but did not differ from beta lactams.

Case fatality risk for BRD

For the CFRBRD model, all variables except initial BRD treatment day-of-week ($P = 0.12$) were significantly ($P \leq 0.01$) associated with the BRD-specific post-treatment deaths (Table 2). Heifers had higher CFRBRD (6.1 ± 1.0) compared to steers (5.1% ± 0.8). Cattle in the 2 heaviest arrival weight categories (900-999, 1,000-1,100 lbs.; 408.3-453.6, 453.7-499.0 kg) had lower CFRBRD when compared to all categories except 500-599 lbs. (226.8-272.2 kg) which did not differ in CFRBRD risk from any category. The month cattle arrived at the feedyard was associated with CFRBRD but no statistical ($P \leq 0.05$) differences among arrival months were identified. Cattle treated in the first 10 days on feed had higher CFRBRD (8.2% ± 1.3) compared to other treatment DOF categories but did not differ from cattle treated at > 100 DOF (7.2% ± 1.2). Rectal temperature at initial treatment < 103 °F (39.4 °C) had the lowest CFRBRD (3.3% ± 0.6) compared to all other categories. Initial treatment with tetracyclines was associated with the lowest CFRBRD (3.5% ± 0.6) compared to all other categories.

Discussion

Outcomes following treatment influence refining therapeutic and disease management plans. The study objective was to identify potential arrival and initial BRD factors that may be associated with 3 major outcomes: FTS, CFRALL and CFRBRD. Overall calculations of each outcome identified a baseline expectation for each outcome. The baseline risk for CFRBRD was lower than CFRALL as expected when utilizing a more specific case definition. Multivariable analysis of the retrospective data revealed many risk factors significantly associated with each outcome of interest. Improved understanding of expected outcomes based on cattle demographic and treatment information allows the inclusion of more variables that impact BRD treatment success when evaluating therapeutic protocols after initial BRD treatment in specific types of cattle.

Risk of death following treatment (CFRALL and CFRBRD) was higher in heifers, but FTS was not associated with sex. This finding agrees with research illustrating that overall feedyard mortality risk may be higher in heifers than steers;[18,19] however, some research shows the actual level of mortality risk by sex is also influenced by arrival weight and time of year of arrival.[6] These previous studies evaluated the overall mortality risk and the current work is only evaluating the post-BRD treatment mortality risk. Heifers have been associated with higher risk of frequently fatal diseases such as acute interstitial pneumonia,[20] but it is unknown the role this disease syndrome may have played in findings from the current study which focused on BRD. Results indicate expectations for fatality risk should be higher in heifers compared to steers after

Table 1: Frequency distribution of cattle initially treated for bovine respiratory disease (BRD) (n = 132,521) in 14 U.S. feedyards between May 2017 and December 2020 among levels of each arrival cohort and initial BRD treatment event characteristic. Arrival information represents data collected at feedyard arrival at the cohort-level and initial event includes individual-animal data collected at the time of the first treatment for BRD.

Arrival characteristics		
Sex	**n**	**Percent of total**
Steers	98,401	74.3%
Heifers	34,120	25.7%
Average Cohort Arrival Weight category		
226.8-272.2	2,575	1.9%
272.3-317.5	6,858	5.2%
317.6-362.9	28,230	21.3%
363.0-408.2	42,570	32.1%
408.3-453.6	37,608	28.4%
453.7-499.0	14,680	11.1%
Cohort arrival month		
Jan	12,997	9.8%
Feb	9,408	7.1%
Mar	7,879	5.9%
Apr	5,976	4.5%
May	7,904	6.0%
Jun	7,920	6.0%
Jul	10,174	7.7%
Aug	12,896	9.7%
Sep	16,016	12.1%
Oct	16,077	12.1%
Nov	11,784	8.9%
Dec	13,490	10.2%

Initial BRD Treatment Event characteristics		
Event DOF category	**n**	**Percent of total**
0-10	15,623	11.8%
11-20	31,269	23.6%
21-30	22,463	17.0%
31-40	16,274	12.3%
41-50	11,507	8.7%
51-60	9,136	6.9%
61-70	6,718	5.1%
71-80	5,185	3.9%
81-90	3,862	2.9%
91-100	2,803	2.1%
> 100	7,681	5.8%
Event rectal temperature		
< 39.4	29,223	22.1%
39.4 – 40.0	12,003	9.1%
40.1 – 40.6	59,500	44.9%
40.7 – 41.1	26,332	19.9%
> 41.1	5,463	4.1%
Event day of week		
Mon	19,448	14.7%
Tue	18,928	14.3%
Wed	20,013	15.1%
Thu	19,368	14.6%
Fri	20,012	15.1%
Sat	17,409	13.1%
Sun	17,343	13.1%
Initial event antibiotic class		
Beta lactam	469	0.4%
Fluoroquinolone	4,030	3.0%
Macrolide	90,622	68.4%
Phenicol	2,457	1.9%
Tetracycline	34,943	26.4%

Table 2: Model-adjusted probability estimates and statistics from multivariable models for each post-initial bovine respiratory disease (BRD) treatment outcome (first treatment success, FTS; non-cause specific case fatality, CFRALL; and post-treatment deaths attributed to BRD, CFRBRD). Each model included random effects for cohort and feedyard. Data (n = 132,521) included cattle initially treated for BRD in 14 U.S. feedyards between May 2017 and December 2020. Differing superscripts among levels of each covariate indicate significant ($P < 0.05$) differences among model estimated probabilities.

	FTS			CFRALL			CFRBRD		
	Main effect *P*-value			Main effect *P*-value			Main effect *P*-value		
	Prob		SE	Prob		SE	Prob		SE
Sex	0.13			< 0.01			< 0.01		
Steers				0.103	a	0.010	0.051	a	0.008
Heifers				0.118	b	0.012	0.062	b	0.010
Arrival weight category	< 0.01			< 0.01			< 0.01		
226.8-272.2	0.664	de	0.014	0.108	ab	0.014	0.054	ab	0.010
272.3-317.5	0.535	a	0.012	0.115	ab	0.013	0.065	b	0.011
317.6-362.9	0.576	b	0.008	0.116	bc	0.012	0.061	b	0.010
363.0-408.2	0.601	c	0.007	0.117	b	0.012	0.062	b	0.010
408.3-453.6	0.636	d	0.007	0.106	ac	0.011	0.052	a	0.009
453.7-499.0	0.660	e	0.008	0.100	a	0.011	0.048	a	0.008
Arrival month	< 0.01			< 0.01			0.04		
Jan	0.596	ab	0.010	0.125	b	0.013	0.063	a	0.011
Feb	0.588	bd	0.011	0.126	b	0.014	0.061	a	0.010
Mar	0.613	abe	0.011	0.108	ab	0.012	0.055	a	0.009
Apr	0.593	ab	0.011	0.110	ab	0.012	0.054	a	0.009
May	0.581	b	0.010	0.113	ab	0.012	0.061	a	0.010
Jun	0.588	bd	0.011	0.110	ab	0.012	0.057	a	0.010
Jul	0.628	ac	0.010	0.105	ab	0.011	0.054	a	0.009
Aug	0.632	ce	0.009	0.102	a	0.011	0.051	a	0.009
Sep	0.662	f	0.008	0.101	a	0.011	0.052	a	0.009
Oct	0.650	cf	0.009	0.101	a	0.011	0.054	a	0.009
Nov	0.624	acd	0.010	0.111	ab	0.012	0.060	a	0.010
Dec	0.596	ab	0.010	0.114	ab	0.012	0.058	a	0.010
Event DOF category	< 0.01			< 0.01			< 0.01		
0-10	0.492	b	0.008	0.125	df	0.013	0.082	d	0.013
11-20	0.553	a	0.008	0.113	e	0.011	0.070	c	0.011
21-30	0.595	c	0.008	0.100	bc	0.010	0.056	b	0.009
31-40	0.633	d	0.008	0.086	a	0.009	0.047	a	0.008
41-50	0.646	df	0.008	0.085	a	0.009	0.045	a	0.008
51-60	0.677	e	0.008	0.087	ab	0.009	0.045	a	0.008
61-70	0.666	ef	0.009	0.093	ac	0.010	0.047	ab	0.008
71-80	0.657	de	0.010	0.107	cde	0.012	0.052	ab	0.009
81-90	0.646	de	0.011	0.114	cde	0.013	0.055	ab	0.010
91-100	0.623	cd	0.012	0.144	f	0.016	0.062	bc	0.011
> 100	0.540	a	0.009	0.191	g	0.018	0.072	cd	0.012

(Table 2 Cont'd):

Event rectal temperature	< 0.01			< 0.01			< 0.01		
< 39.4	0.663	d	0.007	0.073	a	0.008	0.033	a	0.006
39.4 – 40.0	0.578	b	0.008	0.153	d	0.015	0.092	d	0.015
40.1 – 40.6	0.628	c	0.007	0.100	b	0.010	0.051	b	0.008
40.7 – 41.1	0.591	ab	0.007	0.135	c	0.013	0.076	c	0.012
> 41.1	0.603	a	0.010	0.106	b	0.012	0.048	b	0.008
Event day of week	< 0.01			< 0.01			0.12		
Mon	0.607	ab	0.008	0.107	ab	0.011			
Tue	0.610	ab	0.008	0.112	ab	0.011			
Wed	0.605	a	0.008	0.110	ab	0.011			
Thu	0.622	b	0.008	0.113	ab	0.011			
Fri	0.623	b	0.007	0.103	a	0.011			
Sat	0.609	ab	0.008	0.111	ab	0.011			
Sun	0.613	ab	0.008	0.117	b	0.012			
Initial event antibiotic class	< 0.01			< 0.01			< 0.01		
Beta lactam	0.535	a	0.025	0.100	ab	0.016	0.062	bc	0.014
Fluoroquinolone	0.495	a	0.010	0.157	c	0.015	0.073	c	0.012
Macrolide	0.699	c	0.004	0.111	b	0.011	0.056	b	0.009
Phenicol	0.629	b	0.014	0.120	b	0.015	0.063	bc	0.011
Tetracycline	0.691	c	0.004	0.077	a	0.008	0.035	a	0.006

first treatment for BRD.

Mean cohort arrival weight is a commonly used risk factor to predict level of morbidity in groups of cattle with lower arrival weights generally considered to be at higher risk for BRD.[7,21] This study evaluated likelihood of each outcome based on arrival weight and found greatest treatment success and lower risk of mortality in heavier weight classes. This finding agrees with previous research indicating that the likelihood of not finishing the feeding phase following BRD treatment tended to decrease as arrival weight increased.[14] Similar findings were presented when evaluating the likelihood of treatment failure although weights were grouped in broad categories and the effect was modified by days on feed at first treatment.[17] The change in mortality risk following treatment was not linear in either CFRALL or CFRBRD with the 2 heaviest weight categories showing differences from the middle and lower weight categories. Weight is often considered a proxy for age and cattle in the top weight categories (> 900 lbs.; 408.3 kg) were likely older animals and potentially more resilient to disease challenge through prior exposure or immune system development. For FTS, the likelihood of success increased in a stepwise fashion for the 5 categories starting with 600-699 lbs. (272.3-317.5 kg). This impact could be due to the same reasons as changes described for CFRALL/CFRBRD. Additionally, lighter weight cattle would potentially have longer at-risk periods during which additional treatments could be administered.

Arrival month was associated with all 3 outcomes with fall months (Sep, Oct, Nov) displaying some of the higher FTS and lowest CFRALL. This effect contrasts with previous research on the overall risk of BRD which indicates the fall and winter of the year as a prevalent time for BRD risk and period of higher mortality.[6,7,22] Previous work evaluated overall morbidity or mortality risk while the current study evaluates the post-BRD treatment outcomes which represents a different group of individuals than the population as a whole. Decreased post-treatment failure risk during this period could be related to the lack of diagnostic specificity when identifying BRD cases.[23] Diagnostic specificity should not change based on prevalence; however, in BRD outbreaks health observers could be more aggressive in identifying cases resulting in higher level of false positive diagnoses. The potential for more false positive BRD diagnoses during this period may be supported by the fact that when a more specific mortality diagnosis was used (CFRBRD) no statistical differences among individual months were identified.

The timing of initial treatment relative to feedyard arrival was associated with all 3 outcomes and displayed a similar pattern with lower FTS, higher CFRALL and higher CFRBRD both early and late in the feeding phase. Initial treatment timing may be affected by the metaphylactic status of cattle which was not included in this study. This finding is similar to previous research that identified higher likelihood of treatment failure in the first 20 days on feed when all cattle treated after 40 DOF were grouped into a single category.[17] Additional research has also illustrated that in a population of cattle treated for BRD, cattle that subsequently died were treated earlier in the

feeding phase (least squares mean +/- standard error 15 +/- 2.3 DOF) compared to cattle that did not die (22 +/- 0.8 DOF).[12] The early feeding phase is the most common time period for BRD occurrence,[24,25] and during this time period, cattle are often transitioning to new rations, social environments, and housing conditions. This accumulation of risk factors makes disease response challenging. However, these risk factors are not necessarily at play later in the feeding period where we also saw an increase in CFRALL and CFRBRD coupled with the decrease in FTS late in the feeding phase (> 100 DOF). These findings may be related to a change in the prevalence of different pulmonary disease syndromes. While all cases were diagnosed with BRD, the clinical signs would be nearly impossible to distinguish from acute interstitial pneumonia (AIP). Later in the feeding phase is a more common time for AIP occurrence, and risk of fatality from this syndrome is higher than expected from BRD alone.[20,26] These results indicate that expectations for treatment success and mortality should be tempered with the timing of initial BRD treatment.

Rectal temperature at the time of initial BRD treatment was associated with all 3 outcomes, but no discernable trends were identified. Both measures of fatality (CFRALL and CFRBRD) displayed the highest mortality in the 103.0-103.9 °F (39.4-40.0 °C) category which contrasts with previous research illustrating the likelihood of not finishing the feeding phase increased with higher rectal temperatures.[14] Potential reasons for this discrepancy include differences in the method of categorization of rectal temperature and surveys of cattle from different time periods, cattle types and employees.[14] Interestingly, the CFRALL and CFRBRD were lower in the highest temperature category (> 106 °F, 41.1 °C) compared to many other categories evaluated. This could occur if other syndromes beyond BRD were contributing to the fever response, or if the cattle diagnosed in this temperature category were early in the disease process and responded well to treatment.

The day of the week was hypothesized to be associated with treatment outcomes based on changes in labor management during the week. While feedyards are in operation 7 days a week, the weekends are often staffed at a different level and work hours by week-day may vary. While FTS was associated with day of the week at initial BRD treatment, few biological differences were noted. The CFRALL was also associated with day of the week, but the only 2 days that differed indicated that Fridays had lower CFRALL compared to Sundays.

Drug class was recorded at the time of treatment and was associated with all 3 outcomes. These findings should be interpreted cautiously as antimicrobial selection at the time of BRD treatment is often dictated by protocols which may vary by type of cattle, severity of illness, time of year, and other individual feedyard factors. The main reason for including antimicrobial drug class was not in an attempt to evaluate differences in drug classes, as these applications were biased and not randomly assigned, but rather to include this effect in the multivariable models to allow more complete evaluation of the other potential risk factors.

Limitations of this study are primarily associated with the retrospective nature of data collection and analysis. While these findings have good external validity, all potential sources of bias cannot be evaluated or controlled due to the non-random nature of cattle in each demographic group. Additionally, data were collected from multiple production operations and while this impact was controlled for in the analysis with random effects, there are likely still differences among individual operations. Results from this study form a basis for future hypotheses which may need to be further evaluated through subsequent randomized controlled clinical trials.

Another major limitation of this study is the unknown status of metaphylaxis in these cattle. Metaphylactic administration of antimicrobials at arrival may have impacted treatment responses; as for cattle receiving an initial treatment for BRD that received metaphylaxis, this could have been their second dose of antimicrobials after feedyard arrival. Data were unavailable to determine metaphylaxis status; therefore, the impact of this procedure could not be evaluated. Further studies would be useful to help determine if metaphylaxis administration is associated with BRD treatment outcomes.

Conclusions

This study illustrated that several arrival cattle demographics and initial BRD treatment factors were associated with the probability of post-therapeutic success and mortality. Heifers were more likely to die following treatment when measured by CFRALL and CFRBRD. Negative outcomes for all 3 variables were in general more likely in lighter cattle (< 900 lbs.; < 408.2 kg), cattle early (< 20 DOF) and late (> 90 DOF) in the feeding phase. Findings from this research can be useful in setting refined benchmarks for expectations following the initial treatment for BRD.

Funding

This work was funded through an Elanco Animal Health Grant.

End notes

[a]R Studio Version 2023.12.1.402. RStudio Team (2020). RStudio: Integrated Development for R. RStudio, PBC, Boston, MA **http://www.rstudio.com/**

References

1. NAHMS. Health and Health Management on U.S. Feedlots with a Capacity of 1,000 or More Head. 2011. Available at: **https://www.aphis.usda.gov/animal_health/nahms/feedlot/downloads/feedlot2011/Feed11_dr_PartIV_1.pdf**.

2. Johnson KK, Pendell DL. Market impacts of reducing the prevalence of bovine respiratory disease in United States beef cattle feedlots. *Front Vet Sci* 2017;4:189.

3. Miles DG. Overview of the North American beef cattle industry and the incidence of bovine respiratory disease (BRD). *Anim Health Res Rev* 2009;10:101–103.

4. Rojas HA, White BJ, Amrine DE, et al. Predicting bovine respiratory disease risk in feedlot cattle in the first 45 days post arrival. *Pathogens* 2022;11:442.

5. Reinhardt CD, Busby WD, Corah LR. Relationship of various incoming cattle traits with feedlot performance and carcass traits. *J Anim Sci* 2009;87:3030–3042.

6. Babcock AH, Cernicchiaro N, White BJ, et al. A multivariable assessment quantifying effects of cohort-level factors associated with combined mortality and culling risk in cohorts of U.S. commercial feedlot cattle. *Prev Vet Med* 2013;108:38–46.

7. Cernicchiaro N, White BJ, Renter DG, et al. Associations between the distance traveled from sale barns to commercial feedlots in the United States and overall performance, risk of respiratory disease, and cumulative mortality in feeder cattle during 1997 to 2009. *J Anim Sci* 2012;90:1929–1939.

8. Blakebrough-Hall C, McMeniman JP, González LA. An evaluation of the economic effects of bovine respiratory disease on animal performance, carcass traits, and economic outcomes in feedlot cattle defined using four BRD diagnosis methods. *J Anim Sci* 2020;98:skaa005.

9. Cernicchiaro N, White BJ, Renter DG, et al. Evaluation of economic and performance outcomes associated with the number of treatments after an initial diagnosis of bovine respiratory disease in commercial feeder cattle. *Am J Vet Res* 2013;74:300–309.

10. Smith RA. Impact of disease on feedlot performance: a review. *J Anim Sci* 1998;76:272.

11. Booker CW, Lubbers BV. Bovine respiratory disease treatment failure: Impact and potential causes. *Vet Clin North Am Food Anim Pract* 2020;36:487–496.

12. Blakebrough-Hall C, Hick P, Mahony TJ, et al. Factors associated with bovine respiratory disease case fatality in feedlot cattle. *J Anim Sci* 2022;100:skab361.

13. Blakebrough-Hall C, Hick P, González LA. Predicting bovine respiratory disease outcome in feedlot cattle using latent class analysis. *J Anim Sci* 2020;98:skaa381.

14. Theurer ME, White BJ, Larson RL, et al. Relationship between rectal temperature at first treatment for bovine respiratory disease complex in feedlot calves and the probability of not finishing the production cycle. *J Am Vet Med Assoc* 2014;245:1279–1285.

15. Li J, Zhu Y, Shoemake B, et al. A systematic review of the utility of biomarkers as aids in the early diagnosis and outcome prediction of bovine respiratory disease complex in feedlot cattle. *J Vet Diagn Invest* 2022:10406387221081232.

16. Baruch J, Cernicchiaro N, Cull CA, et al. Performance of multiple diagnostic methods in assessing the progression of bovine respiratory disease in calves challenged with infectious bovine rhinotracheitis virus and *Mannheimia haemolytica*. *J Anim Sci* 2019;97:2357–2367.

17. Avra TD, Abell KM, Shane DD, et al. A retrospective analysis of risk factors associated with bovine respiratory disease treatment failure in feedlot cattle. *J Anim Sci* 2017;95:1521.

18. Vogel GJ, Bokenkroger CD, Rutten-Ramos SC. A retrospective evaluation of animal mortality in US feedlots: rate, timing, and cause of death. *Am Assoc Bov Pract* 2015;49:11.

19. Loneragan GH, Dargatz DA, Morley PS, et al. Trends in mortality ratios among cattle in US feedlots. *J Am Vet Med Assoc* 2001;219:1122–1127.

20. Woolums AR, Loneragan GH, Hawkins LL, et al. A survey of the relationship between management practices and risk of acute interstitial pneumonia at US feedlots. *Bov Pract* 2005;32:125–133.

21. Taylor JD, Fulton RW, Lehenbauer TW, et al. The epidemiology of bovine respiratory disease: What is the evidence for predisposing factors? *Can Vet J* 2010;51:1095–1102.

22. Hay KE, Morton JM, Clements ACA, et al. Population-level effects of risk factors for bovine respiratory disease in Australian feedlot cattle. *Prev Vet Med* 2017;140:78–86.

23. Timsit E, Dendukuri N, Schiller I, et al. Diagnostic accuracy of clinical illness for bovine respiratory disease (BRD) diagnosis in beef cattle placed in feedlots: A systematic literature review and hierarchical Bayesian latent-class meta-analysis. *Prev Vet Med* 2016;135:67–73.

24. Babcock AH, Renter DG, White BJ, et al. Temporal distributions of respiratory disease events within cohorts of feedlot cattle and associations with cattle health and performance indices. *Prev Vet Med* 2010;97:198–219.

25. Johnson B, White B, Lancaster P, et al. An evaluation of temporal distributions of high, low, and zero cohort morbidity of cumulative first treatment bovine respiratory disease and their associations with demographic, health, and performance outcomes in US feedlot cattle. *Vet Sci* 2023;10:89.

26. Haydock LAJ, Fenton RK, Smerek D, et al. Bronchopneumonia with interstitial pneumonia in feedlot cattle: Epidemiologic characteristics of affected animals. *Vet Pathol* 2023:03009858221146096.

