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A field study evaluating health, performance, and behavior differences in crossbred beef calves administered different vaccine-parasiticide product combinations☆

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ABSTRACT

Bovine respiratory disease complex (BRDC) is the most important health issue in beef feeder calves. Our study was a randomized, blinded field trial to evaluate potential differences in health, production and behavior in feeder calves administered two different preventive health programs. Calves in two replicates ($n = 308$ and $n = 305$) were allocated to pens and then pens were randomly assigned a preventive health program. One program (Prog1) consisted of 1 injectable clostridial vaccine, 1 intranasal modified live respiratory vaccine, 1 topical and 1 oral parasiticide. The other program (Prog2) consisted of 1 injectable clostridial vaccine, 1 modified live respiratory vaccine and 1 injectable parasiticide. A greater percentage of calves in Prog1 (59.7%) experienced BRDC morbidity compared to the Prog2 program (47.8%). There were no differences between programs in mortality, case fatality, 1st treatment success or chronicity risks. The average daily gain over the entire study period for the Prog2 calves (1.23 kg) was greater than the Prog1 calves (1.16 kg). Calves administered Prog1 on average took more steps each day during the first 28 days of the study. Additionally, Prog1 calves spent more time lying down on certain days during the last 14 days of the study. During initial program administration, fewer Prog1 calves (39.8%) vocalized compared to Prog2 calves (47.8%). In this study, calves administered a program with fewer injections indicated less aversion to program administration than those administered more injections, but experienced greater morbidity and poorer performance.

1. Introduction

Bovine respiratory disease complex (BRDC) continues to be the most economically important disease in post-weaned calves [1–3]. The negative economic effects include reduced performance, increased treatment and labor expense, and reduced carcass quality [4–7]. This disease complex is believed to be multifactorial with components that include viruses, bacteria, stressors, environment and genetics [8–10]. Primarily due to the complex nature of this disease complex, BRDC has been shown to be increasing in frequency despite the creation of new immunization and metaphylaxis regimes [11]. One challenge for controlling BRDC is the few objective clinical disease recognition measures that exist [12]. Some studies have shown that the number of calves treated for BRDC is much lower than the number with pulmonary lesions at slaughter [13]. This suggests that inadequacies in BRDC identification exist, and have increased the need to find effective preventive programs, and numerous studies investigating the individual components of these control programs have been completed. For example, various vaccine types including modified live and killed products, vaccine combinations and timing of vaccine administration, have been investigated as potential BRDC control program components [14–19]. In addition, dietary components such as roughage, concentrate, protein percentage and mineral/vitamin concentration have been investigated as possible control program components [20–24].

The objective of this study was to evaluate potential differences in health, performance and behavior between two feeder-calf arrival health programs differing based on products and number of injections: one program (Prog1; 1 oral, 1 intra nasal, 1 topical, 1 subcutaneous injection) and another program (Prog2; 2 subcutaneous and 1 intramuscular injection). We hypothesized that calves administered the program with fewer injections may behave differently and outperform, both in health and performance, calves administered a more invasive program. This research is unique as it compares overall preventive health programs (including products

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and methods of administration) with respect to health, performance and behavioral outcomes.

2. Materials and methods

This experimental protocol was approved by the Kansas State University Animal Care and Use Committee (Protocol #2571).

2.1. Animals

This study was completed in two replicates using crossbred beef calves. Calves were procured in the Southeast United States (Tennessee and Kentucky) through livestock order-buyers, and transported (average distance 1223 km) to the Kansas State University Stocker Unit (KSBSU), Manhattan, Kansas. Each replicate consisted of three truckloads of cattle where one load of approximately 100 calves arrived each day for 3 consecutive days. Each truckload was housed in a separate string consisting of 8 adjacent dry-lot pens.

2.2. Preventive health programs

All products contained in the health programs are commercially available and were administered according to labeled instructions. The minimally invasive program, hereafter referred to as Prog1, consisted of intranasal modified live vaccine including bovine viral diarrhea virus Type I and II, parainfluenza 3 virus, bovine respiratory syncytial virus, and infectious bovine rhinotracheitis virus (Onset 5 IN®, Intervet/Schering Plough Animal Health, DeSoto, KS); an injectable clostridium bacterin, containing *Clostridium chauvoei*, *Clostridium septicum*, *Clostridium novyii*, *Clostridium sordellii*, *Clostridium perfringens* B, C & D (Vision 7® Intervet/Schering Plough Animal Health, DeSoto, KS); oral fendbendazole endo-parasiticide (Safeguard® Intervet/Schering Plough Animal Health, DeSoto, KS) and a topical avermectin endo-ectoparasiticide (Ivomec Pour-On®, Merial, Duluth, GA) (Table 1). The more invasive program, hereafter referred to as (Prog2), consisted of an injectable modified live vaccine including bovine viral diarrhea virus, parainfluenza 3 virus, bovine respiratory syncytial virus, and infectious bovine rhinotracheitis virus (Bovishield Gold 5®, Pfizer Animal Health, New York, NY); an injectable clostridium bacterin containing *C. chauvoei*, *C. septicum*, *C. novyii*, *C. sordellii*, *C. perfringens* C & D (Ultrabac 7® Pfizer Animal Health, New York, NY) and an injectable doramectin endo-ectoparasiticide (Dectomax Injectable® Pfizer Animal Health, New York, NY) (Table 1). In addition on study-day 28, the Prog1 calves were administered the same clostridium vaccine as on arrival (study-day 0), and the Prog2 calves were administered an injectable modified live vaccine containing bovine respiratory syncytial virus (BRSV) (Bovishield BRSV®, Pfizer Animal Health, New York, NY) and the same clostridium vaccine as they received on arrival. The clostridium vaccines for both program groups and the BRSV vaccine for the Prog2 group were re-administered as recommended by the vaccine product label.

2.3. Preventive health program allocation

Upon arrival to the study facility (study-day 0), calves were individually weighed, determined to be a bull or steer, and given a unique ear-tag identifier. Calves were assigned pens using a random number generator in a commercially available software program (Excel®, Microsoft Corporation, Redmond, WA), and pens were balanced for weight and gender. All pen assignments were done within load resulting in eight pens per load (24 pens in each replicate). A coin flip at every other pen was used to allocate the preventive health program (Prog1 or Prog2); the coin indicated the program for the first pen with the subsequent pen receiving the alternate program. Thus, one half the pens within each load were assigned to each program. Four adjacent pens from a single load in each replicate (2 pens of each program) were selected to participate in the behavior monitoring portion of the study. The random number generator was used to assign calves in the behavior monitoring pens to wear both an accelerometer and pedometer ($n = 32$ each replicate), or pedometer only (replicate 1, $n = 20$ and replicate 2, $n = 21$). Equal numbers of accelerometer/pedometer and pedometer only calves were contained in each program group. These numbers were chosen pre-trial considering the number of accelerometers that were available.

2.4. Preventive health program administration

The day after arrival (study-day 0), calves in each load were administered their assigned program, administered metaphylaxis, ear tissue sampled and bulls were surgically castrated without the use of anesthesia. Program details are listed in Table 1. Programs were administered to all calves by the same individual according to labeled directions. Modified live viral vaccines were administered either intranasally as a single dose (2 ml) in the left nostril or intramuscularly (2 ml) in the right cervical region for the Prog1 and Prog2 programs, respectively. Clostridial vaccines were given subcutaneously in the left cervical region, to calves in Prog1 (2 ml) and Prog2 (5 ml) programs. The Prog1 calves received both a topical (500 mg/kg BW) and oral (5 mg/kg BW) parasiticide. Calves in the Prog2 program received a subcutaneous parasiticide (200 mg/kg BW). Castrations for all calves were performed by the same experienced veterinarian using a Newberry knife (Jorgensen Lab, Loveland, Colorado) and White's Double Crush emasculator (Jorgensen Lab, Loveland, Colorado). All calves were given ceftiofur crystalline free acid (Excede®, Pfizer Animal Health, New York, New York) subcutaneously in the base of the right ear, with the dosage (6.6 mg/kg BW) calculated on average load weight. Biopsies were collected from the right ear of each calf for bovine viral diarrhea virus antigen capture ELISA analysis. Twenty-eight days after arrival, calves in both programs were re-vaccinated with clostridial vaccines, and Prog2 calves were also administered a modified live BRSV vaccine (Table 1).

2.5. Feeding program

All ingredients are reported on a dry matter basis. The arrival diet consisted of prairie hay containing 7.0% crude protein and 0.44 mcal/kg NEg and ad libitum water. Beginning 2 days after arrival, the calves were fed a total mixed ration (TMR) consisting of mixed grass hay, alfalfa hay, dry rolled corn, wet corn gluten feed, and a commercial premix pellet (Cargill Animal Nutrition, Minneapolis, Minnesota). This ration was formulated to contain 15.2% crude protein and 1.09 mcal/kg NEg. Beginning on post arrival day 8 and continuing through day 18, calves were fed a TMR incorporating the same ingredients as above, but containing 15.2% crude protein and 1.14 mcal/kg NEg. On day 19 and continuing through the study endpoint, calves were fed a TMR utilizing the same ingredients formulated to contain 14.4% crude protein and 1.20 mcal/kg NEg. Feed bunks were observed and scored twice daily, and the amount of feed not consumed was used as a basis for the amount delivered at the next feeding.

2.6. Vocalization and chute exit score

A single non-blinded evaluator determined whether each calf vocalized or not during program administration, including vaccine and parasiticides. This determination was completed before metaphylaxis or castration processes were initiated, and any vocalization was considered a positive. Additionally, each calf was

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Table 1
Animal health products, by program and study period, used in a study to compare health, performance and behavior between crossbred beef calves.

Arrival						
Program	Clostridial		Respiratory/viral		Parasiticides	
	Product	Dose/route	Product	Dose/route	Product	Dose/route
Prog1[a]	Vision® 7[b]	2 ml/SQ	Onset 5IM®[b]	2 ml/IN	IvomecPour-On®[c] + Safeguard®[b]	25 ml/topical11 ml/oral
Prog2[d]	Ultrabac® 7[e]	5 ml/SQ	Bovishield® Gold 5[e]	2 ml/IM	Dectomax® injectable[e]	25 ml/SQ

Revaccination					
Program	Clostridial		Respiratory/viral		Parasiticides
	Product	Dose/route	Product	Dose/route	
Prog1[a]	Vision® 7[b]	2 ml/SQ	None	–	None
Prog2[d]	Ultrabac® 7[e]	5 ml/SQ	Bovishield® BRSV[e]	2 ml/IM	None

[a] Prog1, minimally invasive program containing 1 injectable component at both arrival and revaccination.
[b] Intervet/Schering Plough Animal Health, Omaha, NE.
[c] Merial, Duluth, GA.
[d] Prog2, more invasive program containing 3 injectable components on arrival and 2 injectable components at revaccination.
[e] Pfizer Animal Health, New York, NY.

assessed a chute exit score (1 walk, 2 trot, 3 run, 4 jump) after program administration by the same non-blinded individual [25].

2.7. Health monitoring

Calves were observed for health status twice a day by animal care givers employed by the production unit (KSBSU). The care givers were blinded to the preventive health program allocation of each pen. Calves with clinical illness score (CIS) greater than 1 (1, normal; 2, mild depression, gaunt; 3, severe depression, labored breathing, ocular/nasal discharge; 4, moribund, near death, little response to human approach) were taken to the working facility for physical examination. Animals with a CIS greater than 1 and a rectal temperature $\geq$40 °C and not presenting of signs indicating non-respiratory disease were given antibiotics according to the production unit's standard operating procedure. The regimen for BRDC treatment was: first illness, florfenicol (Nuflor®) 40 mg/kg; second illness, enrofloxacin (Baytril®) 10 mg/kg, and third illness oxytetracycline (Biomycin® 200) 4 mg/kg. In both replicates combined, 10 total calves were treated for diseases other than respiratory disease (n = 4 for scrotal infection, n = 2 for lameness, n = 2 for diarrhea and n = 2 for keratoconjunctivitis). These 10 calves completely recovered from their illness and remained in the study. No hospital pen was used in this study; all calves were returned to their original pen after physical examination and medication. Calves observed to be ill, examined and administered antibiotics for the third time were designated as chronic and were not medicated again. Health outcomes of interest included morbidity, first treatment success, chronicity, case fatality, and mortality (Table 2).

2.8. Production parameters

Calves were individually weighed on three occasions: arrival (day 1), revaccination (day 28) and study completion (approximately day 42). Average daily gain (ADG), was calculated for three time periods: arrival to day 28, day 28 to study completion, and from arrival to study completion. These 3 time periods will be hereafter be known as arrival, revaccination, and entire study period, respectively. Total as-fed feed delivered to each pen was recorded and used as a proxy for feed intake and to calculate pen-level feed to gain ratios from arrival to study completion. All production parameters, except feed delivered, were analyzed with mortalities removed from the data set and are defined in Table 2.

2.9. Behavioral assessment

Behavior was monitored for all calves within designated pens using pedometers and accelerometers. The pedometers and accelerometers were applied to the right distal metatarsus using a padded self-adhesive neoprene strap. The entire apparatus, including pedometer, accelerometer and batteries, weighed

Table 2
Definition of pen-level health and performance variables used in comparing two preventive health programs for crossbred beef feeder calves.

Variable	Definition
Morbidity	Number of 1st BRDC[a] treatments in each pen/number of animals allocated to each pen
Mortality	Number of BRDC mortalities in each pen/number of animals allocated to each pen
Case fatality	Number of BRDC mortalities that occurred in calves previously designated as BRDC morbid in each pen/number of calves with first treatments occurring in each pen
Chronicity	Number animals treated 3 times/number of animals allocated to each pen
1st treatment success	1 – (number of calves treated for the 2nd time/number of calves treated 1 time) occurring in each pen
Average daily gain (arrival)	(total weight at day 28 – total arrival weight (day) for all animals that survived to closeout)/28 (days)
Average daily gain (revaccination)	(total weight at study completion – total weight of all animals that were alive on day 28)/total days post-day 28
Average daily gain (study)	(total weight at arrival for all calves that were alive at study completion – total arrival weight of all animals)/total number of days
Feed intake to gain ratio (pen-level)	Total feed (as-fed) delivered/(total closeout weight – total arrival weight of survivors)
Feed delivered (per pen/day)	Total feed (as-fed) delivered/number of animals allocated to each treatment

[a] Bovine respiratory disease complex.

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approximately 0.5 kg. All calves within the behavior assessment pens were taken to the working facility once a week to download accelerometer and pedometer data. Because of the time the calves spent away from their pens during the data download days, these data were removed from the data analysis. Data were analyzed for two time periods: (1) arrival processing through study-day 13 and (2) revaccination (day 28) to study completion. These 2 time periods will be referred to as ARR and REVAC, respectively, throughout the manuscript.

Postural assessment (percent time spent standing and lying down) was completed using accelerometers (GP1 Programmable Accelerometer, Sensr, Elkader, Iowa). The accelerometer recorded five variables at 100 readings per second: average acceleration in three axis (X, Y, Z), vector magnitude average, and vector magnitude maximum. A commercial software program (Sensware, Sensr, Elkader, Iowa) was used to average the readings over a 5 s time period. The total time spent each day lying down or standing was calculated using a pre-established algorithm [26]. Pedometers (NL-800 Activity Monitor, New Lifestyles, Lee's Summit, Missouri) were used to measure total steps taken in a 24 h period.

2.10. Statistical analysis

Data were analyzed with a commercial software program (SAS v. 9.1). Logistic regression (generalized linear mixed) models were used to analyze vocalization, and health outcome data. Vocalization models included chute exit-score as a fixed effect to control for possible confounding [27]. Random effects in the logistic models evaluating potential associations between preventative health program and health outcomes included replicate, truckload within replicate and pen within truckload to account for lack of independence among calves [27]. General linear mixed models were used to evaluate potential associations between the preventative health programs and pen-level ADG, ratio of kilograms of feed fed to kilograms of weight gain, and kilograms of feed delivered. Random effects in these models included, replicate, truckload and truckload within replicate. For the cattle which had behavioral measures, only data from calves not becoming morbid during any portion of the trial were used in the analyses. General linear mixed models were used to evaluate potential associations between health program and the total number of steps taken in a 24 h period (pedometer), the study-day relative to arrival or revaccination, and the potential interaction between step counts and study-day; castration data were evaluated in this analysis as a potential confounder. Each model accounted for repeated measurements on calf and the lack of independence between calves within pen and replicate [27]. Mixed effects logistic regression was used to evaluate associations between health programs and the effects of the daily percent of time spent lying (determined by accelerometers), castration, study-day relative to arrival or revaccination, and the potential interaction between percent of time lying and study-day. The two time periods (13 days post arrival and 14 days post-revaccination) were modeled separately and each model included adjustments for repeated measurements on calves and random effects for pen and replicate. A P-value of ≤ 0.05 was considered significant for all models.

3. Results

3.1. Study subjects

The study population for both replicates combined consisted of 308 calves in Prog1 and 305 in Prog2. The breakdown of calves within program by replicate was Prog1 154 and 154 and Prog2 152 and 153 for replicate 1 and 2, respectively. Mean arrival weights were 207.9 kg and 208.0 kg for Prog1 and Prog2 groups, respectively. By program group within replicate 1 the arrival weights were 207.2 kg (Prog1) and 207.5 kg (Prog2) and for replicate 2, 208.7 kg (Prog1) and 208.6 kg (Prog2). The Prog1 group contained 65% bulls (202/308), 100 in the first replicate and 102 in the second replicate, and the Prog2 group contained 66% bulls (202/305), 101 in the first replicate and 101 in the second replicate. One calf in each replicate, both Prog2 calves, was positive for BVDV persistent infection by antigen capture ELISA. These calves were removed from the study and study site on day 2 and 7, for replicate 1 and 2, respectively.

Table 3
Model[a] adjusted percentages, standard errors, and P-values of health outcomes in combined replicates comparing two crossbred beef feeder-calf preventive health programs.

Health outcomes	Program[b]		P-Value
	Prog1	Prog2	
Morbidity	60.0% (7.0)[c]	47.8% (7.3)	0.02
Mortality	1.5% (1.3)	0.8% (0.7)	0.25
Case fatality	2.7% (2.2)	1.9% (1.7)	0.53
Chronic	15.0% (4.0)	10.7% (3.4)	0.24
1st treatment success	60.9% (5.3)	64.4% (5.4)	0.58

[a] Model included replicate, load and pen as random effects.
[b] Prog1, 1 injectable clostridial vaccine, 1 intra nasal modified live respiratory vaccine, 1 topical parasiticide, 1 oral parasticide. Prog2, 1 injectable clostridial vaccine, 1 injectable modified live respiratory vaccine, 1 injectable parasiticide.
[c] Number experiencing health outcome/number at risk (SE).

3.2. Health

Morbidity in replicate 1 was 65.5% (101/154) for Prog1 and 47.8% (84/152) for Prog2. In replicate 2 morbidity was 53.8% (83/154) and 40.5% (62/153) for Prog1 and Prog2, respectively. Mortality for replicate 1 was 2.6% (4/154) and 3.2% (5/152) for Prog1 and Prog2, respectively. Replicate 2 mortality was 4.5% (7/154) for Prog1 and 0.6% (1/53) for Prog2. Case fatality for replicate 1 was Prog1: 3.9% (4/101) and Prog2: 5.9% (5/84). For replicate 2 case fatality was 8.4% (7/83) and 1.6% (1/62), for Prog1 and Prog2, respectively.

There was no significant interactions between preventive health program and replicate; therefore, data from the replicates were combined for final analysis. Morbidity for Prog1 was 59.7% (184/308) and 47.8% (146/305) for Prog2. The percentage of all morbidity that occurred during the first 28 study-days was 92.7% (306/330). The percentage of mortal Prog1 program calves was 3.5% (11/308) and 1.9% (6/305) for Prog2 program calves. Case fatality for the Prog1 group was 5.9% (11/184) and for the Prog2 group 4.1% (6/146). The percentage of calves defined as chronic was 16.8% (31/184) and 11.6% (17/146) for Prog1 and Prog2, respectively. First treatment success for Prog1 was 60.9% (72/184) and for Prog2 was 64.4% (52/146). The multivariable model indicated that morbidity was lower ($P = 0.02$) in Prog2 (47.8%) calves compared to Prog1 (59.7%) (Table 3). There were no significant differences between groups in first treatment success, chronicity, case fatality and mortality (Table 3).

3.3. Performance

The ADG for ARR was 1.24 kg/day and 1.33 kg/day for Prog1 and Prog2, respectively. For REVAC the ADG for Prog1 was 0.98 kg/day and Prog2 was 1.03 kg/day. From arrival to study completion (ENTIRE) was 1.16 kg/day for Prog1 and 1.23 kg/day for Prog2. Average daily gain (kg/day), for ARR period was greater ($P = 0.05$) in Prog2 compared to Prog1 (Table 4). Average daily gain for the revaccination period was not different between programs. For the period from arrival to study completion, average daily gain was greater for Prog2 (1.23 kg) compared to Prog1 (1.16 kg) ($P = 0.04$). No differences were found in feed to gain ratio or feed delivered

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Table 4
Model[a] adjusted average daily gain (ADG) and *P*-values in combined replicates comparing two crossbred beef feeder-calf preventive health programs.

Performance outcome	Program[b]		*P*-Value
	Prog1	Prog2	
ADG: arrival to revaccination (ARR)	1.24 (0.06)[c]	1.33 (0.06)	0.04
ADG: revaccination to study completion (REVAC)	0.98 (0.05)	1.03 (0.05)	0.46
ADG: arrival to study completion (ENTIRE)	1.16 (0.04)	1.23 (0.04)	0.04
Feed to gain ratio (kg)	3.32 (0.62)[d]	3.13 (0.62)	0.72
Feed delivered (kg)	87.60 (1.54)[e]	90.57 (1.54)	0.17

[a] Model included load, replicate as random effects.
[b] Prog1, 1 injectable clostridial vaccine, 1 intra nasal modified live respiratory vaccine, 1 topical parasiticide, 1 oral parasticide. Prog2, 1 injectable clostridial vaccine, 1 injectable modified live respiratory vaccine, 1 injectable parasiticide.
[c] kg/day (SE).
[d] Feed delivered/ADG (SE).
[e] Feed delivered per pen (SE).

between programs. Unadjusted feed to gain ratio was 3.32 kg/kg and 3.13 kg/kg for Prog1 and Prog2, respectively. Feed delivered for Prog1 was 87.60 kg and 90.57 kg for Prog2 (Table 4).

3.4. Behavior

Pedometer data from 4 calves in replicate 1 for the ARR period, and 1 calf in replicate 1 and 4 calves in replicate 2, for the REVAC period, were not used for analysis due to pedometer malfunction. As previously mentioned, data from data downloading days (7, 14, 42) were removed from the analysis. No interaction between program and study-day or replicate was found for either time period. Model estimated mean steps taken per 24 h period during the ARR period, tended to be greater ($P = 0.07$) for the Prog1 calves (2620) compared to the Prog2 calves (2449). There was no difference between mean steps taken during the REVAC period.

For combined replicates, 64 calves wore accelerometers ($n = 32$ in each replicate). Data from calves wearing accelerometers that became morbid (Prog1: $n = 15$; Prog2: $n = 18$) during any portion of the study were removed from behavior analysis. Additionally, data from 2 calves within each program for the REVAC period were removed from the analysis due to accelerometer malfunction and incomplete data capture. For the first replicate 9 Prog1 and Prog2 calves, and for second replicate 9 Prog1 and 9 Prog2 calves were included in the analysis.

For the percentage of time spent lying down, a program by study-day interaction was found for both time periods examined: ARR (Fig. 1) and REVAC (Fig. 2). The Prog2 program calves did spend more time lying down on days 32 and 34 compared to the Prog1 calves (Fig. 2). Fig. 1 shows that the Prog2 calves spent more time lying down during the early study-days within the ARR period, but lying down behavior for the programs became similar later in this period. During the REVAC period, a similar pattern with Prog2 calves lying down more was observed until day 34, when the Prog2 calves time spent lying down decreased and the Prog1 group time spent lying down increased (Fig. 2).

3.5. Vocalization

The percentage of calves vocalizing at initial program administration was less ($P = 0.05$) in Prog1 (39.8%) compared to Prog2 (47.8%). An association between exit score and the probability of vocalizing was found ($P < 0.01$). The percentage of calves vocalizing decreased as each exit score decreased from 1 to 3. The percentage of calves that vocalized were 63.0% (CI 52.8, 72.2), 52.2% (CI 42.7, 61.5) and 34.4% (CI 25.2, 44.8) for exit score 1, 2, and 3 respectively. No difference in vocalization was found between exit score 3 and 4, 27.4% (CI 17.2, 40.8).

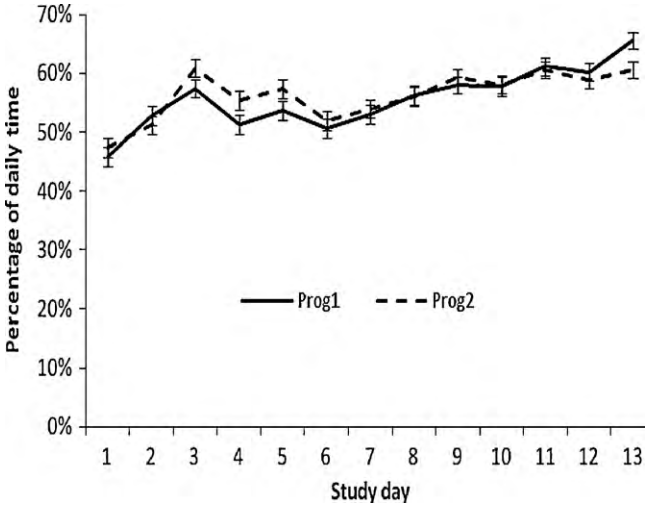

Fig. 1. Model adjusted [Model contained gender, program, study-day, and interactions terms for program by study-day and gender by study-day, and accounted for repeated measurements on calves and random effects of pen (n=)and study replicate ($n = 2$).] mean percentage of time spent lying down for the minimally invasive program (Prog1) and more invasive program (Prog2) preventive health programs for the first 13 days of the study. Prog1 contained 1 injectable vaccination and Prog2 contained 2 injectable vaccines and 1 injectable parasitice. Error bars represent corresponding standard errors.

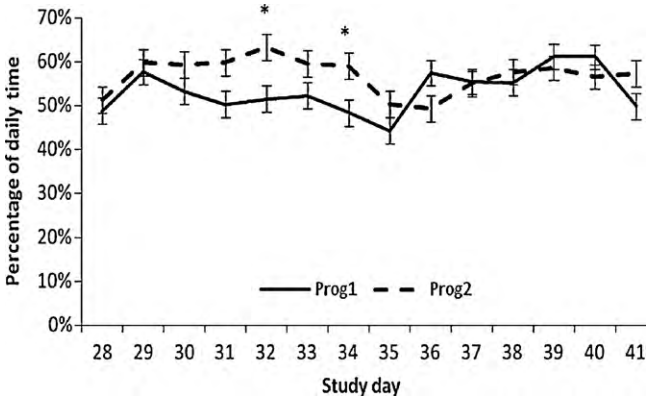

Fig. 2. Model adjusted [Model contained gender, program, study-day, and interactions terms for program by study-day and gender by study-day, and accounted for repeated measurements on calves and random effects of pen (n=) and study replicate ($n = 2$).] mean percentage of time spent lying down for the minimally invasive program (Prog1) and more invasive program (Prog2) preventive health programs from study 28 to study completion. Prog1 contained 1 injectable vaccination and Prog2 contained 2 injectable vaccines and 1 injectable parasitice. Error bars represent corresponding standard errors. *Differences at the $P = 0.05$ level for % time lying down by program and study-day.

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4. Discussion

Calves entering feeder-calf production units are normally administered a combination of preventive health products comprised primarily of vaccines and parasiticide combinations. Although combinations of products are routinely administered, most research studies concentrate on comparing the efficacy of individual products. Our study is unique because two combinations of products were compared, which we have designated "programs". Because we compared programs, the determination of which particular product(s) contributed to the health, performance, and behavioral differences identified in the current research is impossible to determine.

The percentage of calves vocalizing during initial program administration was higher in Prog2 program calves compared to Prog1 calves. The results from our study are similar to a study investigating aversion to injections between calves that were blinded or not-blinded to the presence of humans administering the treatments [28]. This study concluded the injection process is responsible for the aversion demonstrated by the calves and not the mere presence of, or handling by, humans. Other research has indicated that procedures involving the head and ears, such as ear tagging and metaphylaxis administration, result in more frequent vocalization compared to procedures involving only the cervical region [25]. In our study, administration of the Prog1 program did require head manipulation for intranasal vaccine application, but not ear manipulation (vocalization assessment occurred before metaphylaxis was initiated), which may help explain the difference between the two studies.

Neither program appeared to effectively prevent BRDC, but we did not have a negative control group and the level of morbidity was similar to that reported in other beef feeder cattle studies [29,30]. Other researchers have observed differences in BRDC incidence between vaccination combinations [18]. The Prog1 program calves did experience more BRDC morbidity compared to Prog2 calves. Both programs contained vaccines and parasiticides that targeted the same organisms, but differences in route, dosage, and vaccine strains were present. Bovine viral diarrhea virus (BVDV) vaccine strains for Prog1 were Type I: Singer, Type II:125A and for Prog2 were Type I: NADL, Type II: 53637 [31]. Cross reactivity between vaccine and field strains is an important consideration in vaccine selection [31]. In our study, a BVDV persistently infected animal was found in each of two replicates, and transiently BVDV infected animals may have also been present. Although we did not attempt to isolate and characterize strains, it is possible that any BVDV field strains that may have been present were more genomically similar to the strains contained in the Prog2 vaccine and therefore more effective vaccine protection occurred. A difference also existed in the mode of viral vaccine delivery with the Prog1 calves receiving an intranasal vaccine and the Prog2 calves an intramuscular vaccine. Shewen et al. suggest that antibodies to some pathogens produced by mucosal delivered vaccines are transient and do not persist on the mucosal surface without constant antigenic stimulation [32]. Some calves in the Prog1 group may not have been able to maintain long-term mucosal immunity sufficiently to prevent infection.

The parasiticide agents and route of administration also differed between programs, and this may have contributed to the morbidity differences. Internal parasites may negatively impact an animal's ability to mount immune responses to bacterial infections, and studies in mice have demonstrated a negative impact on vaccine efficacy [33,34]. Although previously published information has shown the products used in both programs to be effective in reducing internal parasite populations, parasiticide efficacy in the present study was not evaluated [35–37]. Differences in efficacy of parasiticides between programs may have contributed to our findings.

Although a greater percentage of Prog1 calves became morbid from BRDC compared to Prog2 calves, treatment success outcomes (case fatality, first treatment success, chronicity) did not differ between groups. This suggests the BRDC episodes in the Prog1 group, although more common, were not more severe than those experienced by the Prog2 group.

Calves in the Prog1 program had lower ADG compared to Prog2 calves during the arrival period and over the entire study period. This is not surprising given a greater percentage of Prog1 calves became clinically ill during the trial, and our results are similar to other studies showing BRDC's negative effect on ADG [38,39]. Although there was a difference between preventive health programs in ADG over the entire study period, there was no difference during the revaccination period. Most initial BRDC episodes, and program morbidity differences, occurred during the first 28 study-days (arrival time period), and it would be expected that ADG would be impacted more during this time period relative to the last 14 study-days when morbidity was relatively low. The difference in ADG between Prog2 and Prog1 over the entire study contrasts with no difference found for both feed intake and feed to gain ratio over the same time period. In a different study, dry matter to gain ratio was less for morbid calves compared to non-morbid calves during the first 28 day study period [7]. This discrepancy may be explained by pen size and health-observation intensity. In our study, the pen population was low (11–14 calves) possibly resulting in early BRDC recognition and treatment, which may allow morbid calves' feed intakes to return to normal levels early in the course of disease. Feed conversion results from our study differ with Chirase et al. who showed that calves subcutaneously vaccinated with Vision 7® had lower feed to gain ratio during the first 28 days after arrival to a feedlot compared to calves subcutaneously vaccinated with Ultrabac 7® [40]. In their study morbidity levels were not reported, and no other health products were administered. In our study, morbidity was greater in calves in the program that contained Vision 7® which may have reduced any feed conversion differences that may have existed because of clostridial vaccines. Additionally, because our study compared total health programs and not a single vaccine, other program components may have affected the impact of the *Clostridium* vaccines in a manner differently than was observed in the Chirase study.

Calves administered the more invasive program (Prog2), tended to take fewer steps during the ARRIV period. Because we assessed behavior only in non-morbid calves, this difference is not likely due to the difference in morbidity between groups. Our vocalization results indicated that the Prog2 program was more objectionable, through greater vocalization, and this aversion may have carried over as fewer steps taken into the early portion of the study. The difference in steps may have been an indication of covert lethargy or malaise from the multiple invasive products given on arrival. Because more Prog1 calves experienced morbidity, it is likely more human activity occurred within the Prog1 pens (additional human activity to remove morbid calves from the pen for treatment). Therefore, it is possible that the Prog2 calves did not take fewer steps than expected, but instead the Prog1 calves took more steps due to the additional human activity. This theory is supported by the evidence that no difference in step counts between programs was observed in the REVAC period, when morbidity in both groups was relatively low. Alternatively, the low number of injections (1 or 2) received by each group at revaccination did not elicit a large enough behavioral response to be demonstrated using pedometer data.

A program by study-day interaction for time spent lying down each day was observed in both time periods (ARRIV and REVAC) evaluated in our study. In the ARRIV period, there was separation

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between the estimated time lying on days 3 through 5 post-arrival with the Prog2 calves spending a numerically higher amount of time lying. The Prog1 group experienced more morbidity; therefore, this discrepancy may be explained by a larger number of sub-clinical BRDC cases occurring in the Prog1 group during this time period or additional human interaction as mentioned above. The sub-clinical theory is substantiated by the results from a study where induced *Mannheimia* pneumonia calves spent less time lying down per day after disease onset [12]. Evaluation of 14 days following revaccination (day 28) revealed that calves in the Prog2 program spent more time lying down on days 5 and 7 post-revaccination compared to Prog1 calves. The effect appeared to be transient and no differences were identified after 8 days post-revaccination. Lying behavior in the Prog2 calves may have been due to a transient lethargic response to the higher dose clostridium vaccine and/or the MLV BRSV vaccine. Apley et al. showed an increase in post-vaccination subcutaneous lesion size when comparing 2 ml and 5 ml clostridium vaccines [41]. If lesion size is an indication of inflammatory response, it is possible the Prog2 calves were indicating, by spending more time recumbent, the greater inflammation response to the 5 ml dose clostridium vaccination. The BRSV vaccine may have also played a role in this behavioral response, but previous research did not demonstrate behavioral changes (depression) post BRSV vaccination [42]. However, our study used an objective measure of behavior that may have detected smaller behavioral differences than could be identified through subjective measures.

5. Conclusion

To the authors' knowledge this is the first controlled study comparing two complete feeder-calf health programs and demonstrating differences in some health, production, and behavior outcomes between programs. Fewer calves in the Prog1 program vocalized during initial program administration suggesting programs that incorporate primarily non-injectable products into preventive health regimes are less aversive to calves. Calves in the Prog1 program experienced higher morbidity and lower average daily gain during the early portion of the study and over the entire study period. Calves administered the (Prog1) program tended to take more steps during the early portion of the study. On days after revaccination, the calves administered the more invasive program (Prog2) spent more time lying down. Future research using objective, constant postural monitoring technology, such as accelerometers and pedometers, is needed to gain understanding into calf behavior. Because we compared complete health programs, it is impossible to say which product(s) within each program were responsible for the outcome differences. Because these programs typically contain several components, our study also illustrates the challenges in designing and evaluating new feeder-calf health programs, and the value in utilizing objective measures to evaluate calf behavior as it is affected by these programs.

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