BEHAVIOR VARIABLES OF FEEDLOT CATTLE AS AN EARLY INDICATOR OF BOVINE RESPIRATORY DISEASE

By:

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A Thesis

Submitted in Partial Fulfillment

of the Requirements for the Degree

Masters of Science in Agriculture

Major Subject: Animal Science

West Texas A&M University

Canyon, Texas

December 2015

ABSTRACT

Advancement in technology used to monitor activity in cattle could improve the ability to diagnosis bovine respiratory disease (BRD) in the feedlot as current methods are based on subjective visual assessment of clinical signs that result in low sensitivity and specificity. We hypothesized that cattle affected by BRD express detectable alterations in behavior that can be used to diagnose the disease earlier. Our primary objective was to analyze the association between changes in cattle activity in response to clinical identification of BRD in calves maintained in a commercial feedlot setting. Four arrival blocks of high risk, crossbred beef calves (109 steers, 27.1%, and 293 bulls, 72.9%; initial BW = 176.3 ± 18.8 kg) were received and housed for a 56 d evaluation period at a commercial feedlot (OT Feedyard and Research Center; Easter, TX). The cattle were processed according to standard feedlot protocol and affixed with an accelerometer device (IceQube, IceRobotics, Ltd., Midlothian, Scotland), around the metatarsus of the right rear leg, and continuous activity variables were recorded (standing time, number of steps, number of lying bouts and motion index) relative to clinical BRD diagnosis. Activity data were summarized as daily mean ± standard error for d -6 to -1 relative to the d of clinical BRD diagnosis (d 0). Data were continuously recorded and reported in 15 min intervals and pooled by d for 56 d. Castration status, body weight, and arrival date were recorded at the time of arrival and their effects on clinical BRD morbidity and

mortality rate were analyzed using the Chi-square test. Cases and controls were based on our BRD definition that utilized a combined clinical illness and depression score system. Each case calf's activity was compared with control pen mates (calves that were never BRD-diagnosed during the entire study period) at the same time relative to the disease event. Least squares means of activity variables were calculated and compared between cases and controls within d relative to BRD diagnosis of cases. Additionally, activity variables for d -5 to -3 prior to diagnosis were calculated and compared to the activity on d -1 relative to diagnosis. The percentage of calves diagnosed with BRD at least one time was 49, 23, 62, and 71.6% for block 1, 2, 3 and 4, respectively. Overall, 51.5% of the calves were diagnosed at least once with BRD, while 15.2 and 4.5% had a second and a third BRD diagnosis, respectively, during the 56-d study period. The BRD-associated mortality was 4, 2, 11, and 6.9% for block 1, 2, 3 and 4, respectively, resulting in an overall mortality of 6.0% for the total study period. A trend ($P = 0.10$) was observed for increased BRD morbidity in cattle arriving as bulls (53.9%) compared to those that were steers at the time of arrival (44.9%). Pertinent to arrival BW, a trend for a difference was noted between BW quartiles ($P = 0.06$); cattle in the lower <25% BW quartile averaged a BRD incidence rate of 50.7%, the intermediate 26 to 75% BW quartile averaged 44.8%, and the upper >75% BW quartile averaged 38.7% BRD morbidity rate. Average ± SE standing time on the d prior to diagnosis (d -1) was 559 ± 1.94 min for cases compared to 613 ± 0.32 min in controls. The difference between d -1 and d -5 to -3 for standing time in cases was -26.6 ± 1.5 min compared to 2.33 ± 0.57 min for controls. Similarly, the number of steps on d -1 for cases and controls were 843 ± 7.8 and 1,472 ± 2.2 steps, respectively. The difference in steps between d -1 and d -5 to -3 for BRD cases was -

123.1 ± 4.2 steps compared to 50 ± 2.3 steps in controls. The number of lying bouts for cases and controls was 11.4 and 14.5 on d -1, respectively. The difference between d -1 and d -5 to -3 for lying bouts in cases was -0.58 ± 0.04 min compared to 0.71 ± 0.03 min in controls. These data suggest that cattle that arrive as bulls and cattle in the lighter BW quartiles upon arrival are more prone to be diagnosed with clinical BRD compared to cattle that are steers and those with heavier BW. Furthermore, it was determined that cattle clinically diagnosed with BRD have decreased activity (as expressed by standing duration, steps taken, motion index, and lying bouts) when compared to healthy cohorts and the reduction in these variables was observed several d prior to clinical diagnosis. Accelerometer use as an objective method for diagnosing cattle may assist in the management of clinically ill cattle and provide a framework for understanding the efficacy of cattle behavior as it pertains to clinical BRD diagnoses, potentially improving the sensitivity and specificity of BRD diagnostic methods in the clinical setting.

Key Words: accelerometers, activity, bovine respiratory disease

ACKNOWLEDGEMENTS

None of this would have been possible without the support of so many people, whom I would like to acknowledge and thank at this time. First, I would like to honor my Lord and Savior, Jesus Christ. He has blessed me with so many opportunities that I would never have had the strength to partake by myself. He blesses me constantly with amazing people in my life, an open door to life's next adventure, and an anchor to ride out the waves. Without the Lord in my life, I would not be here, and I owe it all to Him.

Secondly, I would like to thank my major advisor, Dr. John Richeson for taking me on as a graduate student and providing me with incredible opportunities throughout my time at WTAMU. He remains a mentor: encouraging me to stretch my scientific thinking and helping me pay attention to detail. I would also like to thank my co-advisor, Dr. Pablo Pinedo, and the committee member, Dr. Sam Ives, for always being willing to assist and listen to me, be it professional concerns pertaining to my research or personal guidance. Furthermore, I would like to thank them for expending valuable time and efforts to review my thesis and for their willingness to never hesitate to help me conduct research. I would also like to extend my deepest thanks to Tanya Covey and the crew at OT Feed yard, for always being around to help me process cattle, answer questions, and provide me with data and reports from the feed lot.

I would also like to thank my family. My dad, Keith, first for instilling in a love for agriculture and especially cattle and secondly for teaching me the value of education, be it cattle or life related. You taught me the values of hard work, perseverance, and determination all of which are my core strengths to this day. My mom, Barbara, for being my constant friend and my strength throughout the trials of life. Not only is she the shoulder I cry on when my world is shattered by life’s problems but she is also the first to tell me how much she believes in me. Because of you, I learned to believe in myself and that I could be both the strong woman I inspire to be and the compassionate woman that I learned how to be from you. I would not be where I am today without both of your constant love and guidance. And to my brothers, Deven and Breson, who from a very early age provided me the opportunity to both compete with them and laugh with them, two of the most valuable lessons that I have acquired in life.

I would like to take the time to thank those in our Ruminant Health group, who spent countless hours assisting me with my research – Heather Hughes, Shelby Roberts, Clinton Henriod, Sushil Paudyal, and Garrett Bigham. I would also like to thank the personnel at the WTAMU Feedlot. You all have provided me hours of laughs and great memories. Thank you for both being there for me and for helping me through everything. You all have been a superb group to work with. Another huge thanks goes out to my best friend, Kolby Dewbre, for keeping me sane and standing beside me throughout everything. Thank you for being there when I need a friend to get me out of the house or the keeping me company when I needed the motivation to focus and buckle down. You truly are the best and I wouldn’t have gotten this far without you.

Lastly, I would like to thank the AABP foundation for providing the grant to fund my research and for easing the financial burden of acquiring my Masters of Science Degree. Also, a huge thank you is extended to West Texas A&M University for allowing me the opportunity to complete my Masters of Science Degree at such an outstanding and unique university.

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CHAPTER I

INTRODUCTION

Bovine respiratory disease (BRD) complex is the most commonly diagnosed as well as the mostly economically detrimental disease in the feedlot industry in the United States (Moya et. al., 2015; Hilton, 2014; USDA, 2013; Schneider et. al., 2010). Bovine respiratory disease is broadly described as infectious pneumonia with pulmonary lesions. However, BRD is defined more specifically as the result of multifaceted infectious and non-infectious factors and delicately intertwined interactions between different stressors present in the environment, host immunity, and pathogenicity of agents that alter the level of exposure in an individual animal in which at least one bacterial organism is cultured (Muggli-Crockett et. al., 2013; Lamm et. al., 2012; Buckham et. al., 2007; Kahn et. al., 2005).

Despite significant improvements in the efficacy and availability of current prevention, control and treatment technologies, BRD remains the primary cause of morbidity and mortality in feedlot cattle (Woolums et al., 2005). Current BRD diagnostic methods are based largely on subjective visual appraisal of clinical signs such as: depression, lethargy, droopy ears, listlessness, anorexia, decreased body condition, nasal, oral, and ocular discharge, fever, cough, increased or abnormal respiratory rate, and dyspnea. This strategy has remained unchanged over the last several decades and sensitivity and specificity of current field diagnostic methods are estimated to be 61.8 and

62.8%, respectively (White and Renter, 2009). A critical factor in BRD control is timely diagnosis and identification of clinical signs, however, trained personnel are becoming a rare commodity to the cattle feeding industry. Inability of the cowboy to make accurate diagnoses may be influenced by the nature that cattle, being prey animals, possess the desire to disguise sickness and vulnerability (Moya et. al., 2015; McGuirk, 2014; Hanzlicek, 2010; Snowder et. al., 2006).

A measurable, reliable, and repeatable means of field diagnosis that can accurately identify BRD in a cost effective manner is warranted (Tennant et. al., 2014; Muggli-Crockett et. al., 2013). With new technology such as accelerometers capable of continuous monitoring, advancements can be made in the understanding of activity relative to cattle health status and performance. Accelerometers and other technological tools may possess commercial application and potentially decrease time needed to more accurately diagnose BRD morbidity in the commercial production setting.

CHAPTER II

REVIEW OF LITERATURE

Bovine Respiratory Disease Complex

Bovine respiratory disease (BRD) complex is the most economically detrimental cattle disease to feedlots as a result of increased morbidity and mortality rates in cattle (Moya et. al., 2015; Hilton, 2014; USDA, 2013; Woolums et al., 2005). Approximately 75% of total morbidity and 50% of total mortality in commercial feeding operations are attributed to BRD (Hilton, 2014; Tennant et. al., 2014; Richeson et. al., 2013; Loneragan et. al., 2001; Lillie, 1974). Predisposing factors, alone or in combination, include source, previous health history, commingling, fasting and dehydration during transportation, transport distance, change in diet, arrival weight, age, and maturity, genetics, change in environment, pre arrival health management, and feedlot personnel (Moya et. al., 2015; Tennant et. al., 2014; Richeson et. al., 2012; Duff et. al., 2007).

The presence of stressors alters immune function, increasing susceptibility to BRD and other diseases (Moya et. al., 2015). The greatest risk for BRD typically occurs within the first 3 weeks subsequent to arrival, thus management of newly received cattle to mitigate immune dysfunction is one of the greatest challenges presented to the industry (Tennant et. al., 2014; Richeson et. al., 2012; Szyszka et. al., 2012). Unfortunately, the efficacy of respiratory vaccinations upon arrival to the feedlot is questionable and as a result a measurable, reliable, accurate, and repeatable means of diagnosis that can accurately identify BRD in a cost-effective manner is warranted (Tennant et. al., 2014; Muggli-Crockett et. al., 2013).

Diagnostic methods

Current diagnostic methods are based largely on subjective visual appraisal and identified by a variety of clinical signs such as: depression, lethargy, droopy ears, listlessness, anorexia, decreased body condition, nasal, oral, and ocular discharge, fever, cough, increased or abnormal respiratory rate, and dyspnea (McGuirk, 2014; Kasimanickam, 2010; Snowder et. al., 2006). While clinical signs indicate that an animal may be clinically ill, none of them are pathognomonic to BRD. Nevertheless, BRD typically becomes the default diagnosis in a commercial setting due to the high prevalence of BRD and the lack of specificity in diagnostic techniques (Tennant et. al., 2014).

Incidence rate

Consequently, the bias towards BRD as the "catch all" diagnosis in the commercial feedlot likely inflates the average overall incidence of BRD, which was estimated to be 14.4% in the overall fed cattle population (NAHMS, 2000a). The overall incidence of BRD is gradually increasing and is currently upwards of 16.2%, resulting in an increased incidence than what was observed 20 yrs ago, despite increased availability of vaccines and antimicrobials intended to prevent and treat the disease (USDA, 2013). Antimicrobials inhibit cell wall, protein, and nucleic acid synthesis as well as attack cell membranes and interfere with metabolism in gram positive and gram negative bacteria.

However, there is no way for current antimicrobials to target specific bacteria and as such current antimicrobials are non-selective, resulting in the lysis of both helpful and harmful bacteria. With the destruction of bacteria, incidentally there is the potential for bacterial growth and colonization, and this could be either helpful or harmful. Thus in some cases, antimicrobials could potentially increase the overall population size of harmful bacteria and this could ultimately play a role in incidence rates.

Trends in mortality ratios were investigated in a retrospective study of 21.8 million head of cattle across 121 United States feedlots through primary body system affected and sex of the animal then calculated into monthly and yearly ratios (Loneragan et. al., 2001). The average mortality ratio was 1.26% or 12.6 deaths for every 1,000 head of cattle on feed and respiratory disorders were noted to have accounted for 57.1% of all deaths accrued in the commercial feedlot setting. Trends were observed for an increased risk of death in dairy-influenced cattle compared to beef breeds and heifers was reported to have an increased mortality risk when compared to steers. Loneragan concluded "although overall yearly mortality ratio did not significantly increase during the study, the risk of death attributable to respiratory tract disorders was increased during most yrs, compared with risk of death during 1994" (Loneragan et. al., 2001). Unfortunately, the results of the study were limited due to the limited nature of the ability to access different factors. Information from the retrospective study was acquired on a voluntary basis and thus is not an accurate representation of all of US feedlots and BRD had the potential to have been over represented due to potential disease misclassification in both morbidity and mortality estimates. Furthermore the mortality rate recovered was derived from a ratio of overall deaths on the yard and likely confounded the month specific mortality ratios reported (Loneragan et. al., 2001).

Predisposing Factors

Several additive predisposing factors contribute to the increased incidence of BRD including age and various physical and psychological stressors: weaning, handling, castration, transportation, commingling, social restructuring, weather, dehydration, nutritional changes, and immune system dysfunction (Hilton, 2014; Richeson et. al., 2013; Snowder et. al., 2006). Predisposing factors not only affect the risk of an animal being diagnosed with BRD but also affect feed intake, growth, behavior, metabolism, carcass composition, and immune system function (Richeson et. al., 2013; Richeson et. al., 2008). The combination of multiple factors attribute to the BRD risk level determined for cattle entering a feedlot; high to low risk. This BRD risk assessment is currently based on limited information such as origin, commingling, transport duration, shrink, and body condition score as well as overall appearance, change in environmental temperature or precipitation, and expertise of management personnel (Richeson et. al., 2013; Richeson et. al., 2008). Cattle that are purchased at auctions are typically considered high risk and often associated with being of unknown origin, commingled, and recently weaned (Richeson et. al., 2008).

The accumulation of several factors increases the probability of providing an ecological niche utilized by viral and bacterial pathogens to increase BRD incidence; viral: infectious bovine rhinotracheitis virus (IBRV), bovine viral diarrhea virus (BVDV), bovine respiratory syncytial virus (BRSV), and parainfluenza-3 virus (PI3V) and bacterial: *Mannheimia haemolytica*, *Pasteurella multocida*, *Haemophilus somnus*, and

Mycoplasma bovis (USDA, 2013; Snowder et. al., 2006; Cusack et. al., 2003, Godson, 1996). Although contributing factors may all be identified, the interaction, the animal's physiological response, and the contribution to BRD are yet to be completely understood (Taylor et. al., 2010; Godson, 1996; Yates et. al., 1982).

Economics

Cattle diagnosed with BRD experience reduced performance expressed by reduced feed intake and growth as well as a negative impact on carcass traits if marketed at the same endpoint as healthy cohorts (Amrine et. al., 2014; Cernicchiaro et. al., 2013; Muggli-Crockett et. al., 2013; USDA, 2013). Griffin (1997) estimated a loss of $750 million annually, excluding lost production, veterinary fees, and death loss, whereas, Hanzlicek et al. (2010) estimated greater than $3 billion, annually, to the cattle industry including prevention and treatment costs. Furthermore, an estimated loss exceeding $4 billion annually, including treatment costs, lost productivity, and prevention costs has been estimated (Griffin, 1997).

As a result, producers incur major economic losses as a direct result of increased mortality, treatment costs, disposal costs and decreased production. It is estimated that production and treatment costs have an impact of $13.90 to $15.57/head, excluding increased labor, handling, extended days on feed (DOF) to reach a similar finishing point compared to healthy cohorts, or metaphylaxis costs (Schneider et. al., 2010; Schneider et. al., 2009; Snowder et. al., 2006). Another investigation estimated a significantly increased average cost of treatment of $27.03 with a decrease in ADG of 0.32 lbs. when compared to healthy cattle (Smith, 2010).

Affected cattle treated once, twice, or thrice returned $40.64, $58.35, and $291.93 less, respectively, than healthy cohorts (Duff et. al., 2007). Schneider delved more intimately into the figures and broke down losses associated with primary, secondary and tertiary treatment ($23.23, $30.15, and $54.01) as well as losses reflected by ADG ($15.76, $22.09, and $46.70) in animals treated one, two, or three times, respectively (Schneider et. al., 2009).

Carcass traits are also negatively affected by BRD by reducing quality grade when compared to healthy cohorts. The percentage of steers grading choice was reduced 12.1% compared to healthy animals and was associated with a decreased return of $87.60 per carcass (Smith, 2010). Compromised carcass traits resulted in a discounted carcass price of $23.23, $30.15, and $54.01 in cattle treated once, twice, and thrice, respectively (Schneider, 2009).

The number of treatments an animal received for BRD and this effect on economic outcome and animal performance in 212,867 head of cattle using a model to estimate net returns and determine associations was recently investigated (Cernicchiaro et. al., 2013). The authors reported that expected returns decreased at an increasing rate as the number of treatments increased and that the expected returns varied with season of arrival. Increased returns were noted in the fall and summer compared to other times of the yr with animals returning $39.41 compared to $31.83 for animals never treated, $29.49 versus $20.22 for cattle treated once, $16.56 in contrast to $6.37 in cattle treated twice, and –$33.00 in comparison to –$42.56 in cattle treated 3 or more times in the fall and summer, respectively. The difference in overall returns was contributed to overall meat quality, indicated by the USDA meat quality grading scale that decreased as number of treatments increased (Cernicchiaro et. al., 2013). The authors concluded that the profit margin for an individual animal decreased as the number of treatments increased which reduced the overall performance of the animal regardless of season of arrival, sex, and arrival weight.

Common management practices and associated stressors

Management practices related to the relocation of cattle and the influence of different stressors that compromise an animal's immune system continue to be an important focus for understanding BRD pathogenesis (Kasimanickam, 2010; Whiteley et. al., 1992). Typical marketing strategies and management practices introduce stress that can predispose an animal to infection and enhance virulence of specific strains of viral or bacterial pathogens causing rapid colonization and proliferation (Kahn et. al., 2005; Whiteley et. al., 1992; Lillie, 1974). Consequently, the majority of BRD occurs within the first 27 d after receiving as a result of increased stressors and their assault on an animal's immunity, thereby enhancing the prevalence and severity of a BRD outbreak during the early receiving period (Muggli-Crockett et. al., 2013; Kasimanickam, 2010; Schneider et. al., 2010). The period of greatest risk for BRD occurs 5 d after arrival and ranges to 80 DOF (Snowder et. al., 2006). Risk factors include: unknown health histories, weaning and processing, marketing, transportation, commingling, ventilation, and environmental factors (Hilton, 2014; Snowder et. al., 2006; Bagley, 1997; Whiteley et. al., 1992).

Weaning management

Weaning of calves from the dam, at approximately 6 to 14 mo of age, concurrent with marketing, is potentially the most stressful time period throughout the entire beef production system as it typically involves an abrupt separation from the dam, termination of nursing, a substantial change in nutrient intake, a change in spatial environment, and social hierarchy reconstruction (Enríquez, et. al., 2011; Boyles et. al., 2007). Conventional weaning practices include early and abrupt weaning and relocation, fence line contact, or use of devices to prevent suckling. This separation involves a combination of both behavioral and physiological stressors (Enríquez, et. al., 2011).

The dam, upon calving, develops a strong maternal bond with the calf, strengthened by licking, suckling, warmth, protection, and development of survival skills. This bond is developed rapidly after birth and the survival of the calf is largely dependent on the strength of this bond (Enríquez, et. al., 2011). Natural weaning of the calf from the cow, occurring when the milk supply is no longer sufficient to meet energy requirements, is a gradual process, resulting in a decreased volume of milk over time coupled with an increase in forage intake which in turn reduces the maternal-filial bond as the dam increasingly rejects nursing attempts stimulating the calf to search for an increased calories from other feed sources (Enríquez, et. al., 2011). Removal from the dam with conventional weaning occurs without completion of the gradual adaptation that naturally occurs.

It is a common practice to relocate calves upon weaning, resulting in a new environment, development of a new social structure, isolation, and a new diet creating an additive stress event. Movement to a new location involves relocation of food, water, and shelter; furthermore, freshly weaned calves are prone to increased vocalization and activity (Enríquez, et. al., 2011). Relocation also increases social interactions with cattle other than the dam, intensified aggression towards pen mates, and more frequent human contact.

Weaning is a necessary and practical practice in the conventional beef system, not only to increase efficiency of the calf but also improve reproductive performance of the dam (Enríquez, et. al., 2011). The development of improved weaning management techniques to reduce acute and chronic stressors, thus, reducing morbidity and mortality rates is gaining popularity within the industry, but this should be supported with scientific evidence of the morphological, physiological, and psychological mechanisms involved in the weaning process as well as be ethically acceptable to society and considerate to the welfare of calves (Enríquez, et. al., 2011). This could be achieved by better matching weaning practices with the natural weaning process by dam with gradual changes in diet and maternal bond and exploration of the new environment prior to weaning.

Because of the multiple stressors associated with current weaning management practices, BRD typically develops in newly weaned calves in a predictable manner soon after arrival at the feedlot (Derosa et. al., 2000). Proper weaning management and vaccination protocols may reduce the risk of BRD morbidity, but preventative measures do not eliminate BRD risk (Cusack et. al., 2003).

In particular, calves with an unknown health history are more likely to succumb to BRD and are likely to receive multiple antimicrobial treatments during the feeding period

(Seeger et. al., 2008). High risk calves are more likely to show clinical signs earlier in the feeding period as well as reduced performance compared to cattle receiving a weaning management health protocol before arrival (Seeger et. al., 2008).

Studies have shown that preconditioning management practices, which includes weaning calves 45 d and administering a respiratory vaccine before shipping, had a reduced morbidity rate (5 and 7.7%, respectively) than recently weaned, single source calves (22.2%) and had significantly improved morbidity rates compared to recently weaned, commingled calves (31.9%; Smith, 2010). Calves that were weaned 45 d before transport also had improved ADG of 0.20 lbs and increased gain to feed efficiency (G:F) of 0.58 lbs relative to feed intake (Smith, 2010). Observed reductions in medical costs ($29.67/animal), reduced cost of gain (COG; $8.05/animal), improvement in death loss (1.3 vs. 4.44%), and an overall net return of $60.72/head in preconditioned calves were evident in the feeding period (Smith, 2010). This indicates that improved management practices result in overall improved health as well as superior performance and suggests that proper weaning management techniques could have a more profound impact to overall animal health than that of vaccination (Richeson et. al., 2012; Step et. al., 2008; Cusack et. al., 2003). However, the segmented beef industry results in inadequate communication between different sectors. Unfortunately, limited economic return to the feedlot producer does not always provide incentives for purchasing more expensive cattle with proper preconditioning protocols and results in weaning management practices to continue to be an important concern for the cattle production industry (Richeson et. al., 2013; Snowder et. al., 2006).

Transportation

The effects of poor weaning management are then amplified by imposing relocation and introducing a combination of added stressors that suppress the animal's immune system resulting in an increased BRD risk and susceptibility (USDA, 2013; Buckham et. al., 2008; Step et. al., 2008; Snowder et. al., 2006; Cusack et. al., 2003; Lillie, 1974). Transportation stress is a well-known, non-infectious phenomenon that affects many aspects within the beef industry, from health to production to animal welfare, and negatively alters an animal's physiological state (Taylor et. al., 2010; Buckham et. al., 2008; Buckham et. al., 2007). The most stressful components of transport was determined to be handling associated with loading, especially in cattle shipped short distances (Cole, 1988). A positive, non-linear association has been identified between the duration of transport and increased morbidity rates, with distance evolving into an adequate predictor of mortality rates with the consideration of the attributes or the livestock being received, such as when region, gender, weight and season are considered (Babcock et al., 2013; Taylor et. al., 2010; Cusack et. al., 2003). This association assists in management decisions as related to BRD treatment and control measures upon arrival, including providing rest periods before initial processing, especially in cattle shipped long distances (Richeson et. al., 2013; Kahn et. al., 2005).

Commingling

Transportation also gives way to commingling, a re-establishment of social hierarchy as new animals are added to produce a purchase group from different sources and regions, and increased stocking density of many animals from different backgrounds also occurs. Commingling is identified as a primary, but often overlooked, contributor to the increased BRD morbidity and mortality rate in beef cattle as it has been associated with an alteration to the immune system and increased exposure to viral and bacterial pathogens (Hilton, 2014; Kasimanickam, 2010; Snowder et. al., 2006; Whiteley et. al., 1992). Approximately 96.8% of large feedlots in the U.S. process cattle from many sources as a group within 24 h of arrival which threatens any biocontainment and increases the probability of transmission of pathogens involved in BRD (USDA, 2013; Duff et. al., 2007).

One investigator evaluated different preconditioning management techniques on 509 head of crossbred steers during a 42 d period after being received at a feedlot and commingled with other cattle with unknown histories in an attempt to explain how growth, performance, and health were affected (Step et. al., 2008). Single source ranch calves, multiple source auction market calves, and a combination of single source and multiple source calves with weaning techniques including direct weaned, weaned 45 d prior to transport, or weaned and vaccinated 45 d prior to transport were randomly assigned in a 2 × 3 + 1 factorial treatment arrangement with market cattle serving as the control. Dry matter intake was not affected by origin, however, calves that were weaned 45 d before transport, regardless of vaccination status, had improved intakes, were treated for BRD less often, and had reduced treatment costs. Calves directly from the ranch had improved ADG and were treated for BRD less often and had reduced treatment costs than commingled cohorts (Step et. al., 2008).

The increase in ADG could be attributed to possible exposure to bunk feeding (Duff et. al., 2007). It was also determined that auction market calves required an increased number of antimicrobial treatments and received treatment earlier in the feeding period when compared to ranch origin cohorts of comparable age and weight, resulting in increased total costs due to increased health costs and a more expensive COG as well as increased mortality in the auction market calves (Taylor et. al., 2010; Step et. al., 2008). It is noted that commingling resulting from the marketing process may directly result in an increased BRD incidence rate rather than the exposure to an auction barn environment (Taylor et. al., 2010).

Trends suggest that as social disruptions increases, production efficiency decreases and morbidity increases. The health advantages seen in single source cattle could be attributed to decreased social stress, reduced pathogen exposure, and fewer stressors (Taylor et. al., 2010; Step et. al., 2008; Duff et. al., 2007). Morbidity and mortality have also been noted to increase when naïve cattle are mixed with cattle previously exposed to BRD-associated pathogens, not only by the infectious agents themselves, but also from the stress inflicted by the rearrangement of the social hierarchy within the herd (Duff et. al., 2007; Cusack et. al., 2003). As the number of sources increase, the likelihood of cattle being diagnosed with BRD increases and thus, commingling could also serve as an indicator of BRD risk and should be considered when making management decisions (Smith, 2010).

Diet Transition

Upon arrival to the feedlot, cattle are typically introduced to a novel diet. It has been suggested that improper diet formulation may contribute to BRD incidence as a result of inadequate energy and true protein intake in stressed cattle (Cusack et. al., 2003). Nonetheless, the ability to manipulate diets to improve BRD incidence is limited (Duff et. al., 2007). Several studies indicate that feeding newly received cattle a diet with high concentrations of forages could potentially result in a slight reduction of BRD incidence; consequently, this also resulted in reduced gains from the reduced energy density of forage compared to high concentrate grain diets (Duff et. al., 2007; Cusack et. al., 2003; Lofgreen, 1983). Conversely, it has been implied that high energy diets could result in slightly increased BRD morbidity rate or total sick days but result in improvements in ADG, dry matter intake (DMI), and G:F (Lofgreen, 1983). Similarly, there is an implied connection between feeding corn silage during the first month and an increase of BRD incidence rate, possibly resulting from limited rumen degradable protein, and increased sugars that corn silage possesses; however, effects can potentially be reduced by adding corn (Taylor et. al., 2010; Cusack et. al., 2003). Feeding of high moisture barley has also been suggested to be linked to BRD mortality (Cusack et. al., 2003). Some scientists have suggested that increasing the crude protein content of the diet also increases BRD, but this is not clear from the literature (Taylor et. al., 2010; Duff et. al., 2007).

It has been reported that a milled diet between 50 to 72% concentrate provides the best nutritional value when combined with a low morbidity rate, but increased concentrates could be detrimental (Taylor et. al., 2010; Duff et. al., 2007). Taylor et al. (2010) reported that increased energy in the diets could be used to improve ADG without a negative effect on morbidity rates. Unfortunately, no general consensus on appropriate ration formulation for high risk arrivals can be elucidated. Insufficient research has been conducted to determine if mineral or vitamin supplementation could have an impact on

BRD (Taylor et. al., 2010; Duff et. al., 2007). Moreover, an agreement on the amount of roughage and the effect on morbidity is yet to be determined and energy concentration does not appear to have a significant impact on overall morbidity, but transmission rate of different bacteria tended to be increased in the greater energy concentration diets (Berry et al., 2004a, b).

Regardless of the conflicting research on diet formulation and BRD morbidity, there is an agreement that animals affected with BRD have reduced ADG (Schneider et. al., 2010; Smith, 2010). It is noted that body weight of chronically infected animals started to decline on d 17 after initial infection as animals started to gain weight at a slower rate than healthy pen mates (Szyszka et. al., 2012). It has also been observed that the number of eating and drinking episodes per d decreased slightly in infected animals although total drinking time was not different (Moya et. al., 2015; Szyszka et. al., 2012). Thus feeding behavior and rumination could be a potential diagnostic tool for BRD in feedlot cattle (Wolfger et. al., 2015).

Host factors and response

Sex

The pathogenesis of BRD is not only affected by the management practices and infectious agents but also natural or inherent traits of individual cattle and how the host responds to the disease (Godson, 1996). Animal gender, breed and genetics, weight and age at arrival, season of arrival, and weather are also associated with the occurrence of BRD in feedlots (Babcock et al., 2013). Steers are more likely to be diagnosed with BRD than heifers, 20 and 14% respectively, and steers experiencing the additional stress of castration upon feedlot arrival are 92% more likely to suffer from morbidity and 3.5% more likely to suffer from mortality then that of previously castrated steers (Snowder et. al., 2006; Duff et. al., 2007). In a retrospective analysis, the odds ratio for bulls being diagnosed with BRD and pulled once were 3.32 times greater and pulled twice were 4.02 times greater than that of steers (Richeson et. al., 2013). Castration increases morbidity and results in increased stress and inflammation, thus, the added stress of castration of bulls upon arrival potentially has a more significant impact on the BRD incidence compared to steers that arrive having been previously castrated and convalesced (Richeson et. al., 2013, Duff et. al., 2007, Snowder et. al., 2006).

Another potential attribute to the increased morbidity in steers could result from “buller” syndrome, or excessive sexual activity by pen mates, resulting in increased stress (Taylor et. al., 2010). On the contrary, heifers have an increased mortality risk versus steers, but there have been reports in which no difference in mortality between sexes was observed (Babcock et al., 2013; Taylor et. al., 2010; Loneragan et. al., 2001). Still, other reports suggest an association between sex and mortality rate (Loneragan et. al., 2001). Heifers are also noted to have significantly decreased ADG and hot carcass weight (HCW) compared to steers (Cernicchiaro et. al., 2013). The effect of gender on BRD outcome is further influenced by arrival weight and season of arrival (Babcock et al., 2013; Cernicchiaro et. al., 2013).

Genetics

Little is understood between genetic attributes and predisposition to BRD; however, considerable advances are being made in long-term breeding programs and genetic selection concerning animal disease resistance (Berry et. al., 2011). Improved genetics could complement current management practices to help reduce BRD incidence and the tools for advanced genetic selection are available (Berry et. al., 2011). "Heritability of BRD susceptibility appears to be low, but breed differences have been detected" (Taylor et. al., 2010). Selecting for BRD resistance within the Angus breed could be the most practical as Angus possess the most manageable unadjusted mean incidence (Schneider et. al., 2010; Taylor et. al., 2010; Snowder et. al., 2006). Charolais and Gelvbieh cattle also have relatively low unadjusted mean incidences (Snowder et. al., 2006). Pinzgauer, Braunvieh, Simmental, and Limousin had relatively high mean incidence rates with Pinzgauers and Limousins possessing the highest incidence rates (Muggli-Crockett et. al., 2013; Snowder et. al., 2006) Similarly, Simmental and Limousin were consistently diagnosed with BRD earlier in the feeding period, whereas Charolais were consistently diagnosed later in the feeding period, and Angus and Braunvieh were diagnosed in the mid-range of the feeding period (Snowder et. al., 2006).

Muggli-Crockett et al. (2013) reported similar results throughout breeds concerning frequency of post weaning BRD: Angus possessed the lowest frequency of BRD, followed by Limousin, Charolais, Gelbvieh, and Pinzgauer, with Braunvieh cattle appearing to have the greatest susceptibility to BRD. Crossbred (hybrid) cattle appear to possess the greatest BRD resistance, and *Bos taurus* breeds are more likely to be diagnosed with BRD than that of *Bos indicus* (Taylor et. al., 2010). Furthermore, dairy influenced breeds maintain a greater risk of death due to BRD when compared to beef cattle (Loneragan et. al., 2001).

Snowder et. al. (2006) attempted to characterize different factors related to the incidence rate of BRD in feedlot calves over a 15 yr period, including genetics, environmental impact, and economic influence utilizing 18,112 cattle records. Records included data from Angus, Braunvieh, Charolais, Gelbvieh, Hereford, Limousin, Pinzgauer, Red Poll, Simmental and 3 composite breeds. Trained personnel recorded BRD incidence and trends were established among the breeds. The incidence rate for BRD ranged from 5 to 44% with an average of 20% incidence noticed before 1992 and falling to below 14% in more recent yrs (Snowder et. al., 2006). Snowder observed that BRD incidence was greatest between 5 through 80 DOF, and incidence increased with castration but was not affected by previous health status. A limited breed variation for BRD incidence was observed; however, Herefords had the greatest susceptibility when compared to composite animals and Red Poll calves experienced the highest mortality rates (Snowder et. al., 2006). Snowder noted that although genetic improvements in BRD resistance could be made, progress would be slow and improvements in management methods are more practical.

Sources vary on the heritability estimates for BRD resistance but typically range from 0.10 to 0.20, with an outlier range of 0.00 to 0.26 and the overall annual heritability trending towards that of 0.17 or 0.18 (Schneider et. al., 2010; Snowder et. al., 2006). Heritability ranges from not heritable (0) to fully heritable (1) and most health traits are considered low to moderately heritable (Berry, 2014). Comparatively, growth traits such as birth weight (0.70), weaning weight (0.46), and yearling weight (0.49) are considered highly heritable, carcass traits like carcass weight (0.40), adjusted back fat thickness (0.36), marbling (0.37), and longissimus muscle area (0.40) are considered to have moderate heritability estimates, and reproductive traits like calving difficulty (0.22 to 0.42), age at first calving (0.01 to 0.27), and heifer pregnancy rate (0.14 to .021) are considered to have moderate to low heritability estimates (Cammack et. al., 2009; Rios et. al., 2004; Knights, et. al., 1984)

Research suggests heritability estimates trend towards the lower end of the range with 0.04 to 0.11 for the maternal component and trend towards the higher end of the range with a 0.70 to 0.22 for the direct component (Berry, 2014; Berry et. al., 2011; Schneider et. al., 2010). The variation in heritability estimates could likely be traced to breed differences and genetic variance and evidence suggests as overall BRD incidence rate increases, so do heritability estimates (Berry, 2014; Schneider et. al., 2010). Low estimates agree with the recognized trend that health traits maintain low heritability, however, improvement is still conceivable (Muggli-Crockett et. al., 2013).

Schneider et al. (2010) evaluated the variance and heritability of BRD in 1,519 pre-weaned calves and 3,277 mature cattle. The authors determined that BRD incidence rates could be estimated as 11.39, 82.1, 13.9, and 4% in pre-weaned calves and animals treated once, twice, and thrice, respectively. Heritability estimates of 0.11 for BRD resistance in pre-weaned calves were obtained and estimates of 0.08 heritability were observed for the number of treatments. Correlation estimates of BRD incidence in relation to weaning body weight (-0.02), and birth weight (0.07), were also reported; a 0.25 and 0.30 correlation was observed between number of treatments for weaning weight or birth weight, respectively. In feedlot cattle, BRD incidence was estimated at 9.43%; and the heritability for BRD incidence was 0.07 and 0.02 for number of treatments, respectively (Schneider et. al., 2010). Undesirable production traits associated with BRD incidence were demonstrated with genetic correlations of -0.31 overall ADG, -0.39 final body weight, -0.22 HCW, -0.03 loin muscle (LM) area, 0.24 fat and -0.43 marbling; number of treatments revealed correlation with production traits of -0.47 overall ADG, -0.66 final BW, -0.58 HCW, -0.12 LM area, 0.42 fat, and -0.32 marbling score. The authors concluded that it was economically feasible to consider the incorporation of the heritability of BRD resistance into beef production management practices (Schneider et. al., 2010).

It can be surmised that developing a selection protocol for BRD resistance in cattle is challenging due to low heritability and this opportunity would require meticulous selection of breeding stock (Schneider et. al., 2010). However, genetic selection for disease resistance could ultimately increase profit from increased performance and carcass merit (Schneider et. al., 2010). Selection for disease resistance would potentially have little to favorable effect on ADG, final body weight, HCW, ribeye area (REA), back fat, and marbling as a result of limited correlation (Schneider et. al., 2010). Differences in pre-weaning and post-weaning BRD frequency and suggestions of heterosis and phenotypic variation indicate that genetics and breeding could be used for BRD resistance (Muggli-Crockett et. al., 2013). Challenges are presented when selection is based upon BRD history but including that of relatives, progeny, and that of other immune traits may improve selection value (Muggli-Crockett et. al., 2013; Berry et. al., 2011). After a genetic marker has been identified, it can be genotyped and potential resistance could be predicted (Berry et. al., 2011). It has also been suggested that using a cross breeding program could also positively affect BRD resistance selection (Muggli-Crockett et. al., 2013). Caution must be maintained as genetic gain is cumulative and permanent, possibly affecting the animal's ability to respond to other diseases; pathogens would simultaneously be evolving and accurate records would need to be kept to monitor unfavorable trends with other diseases (Berry et. al., 2011).

Age and weight

More manageable linked host factors are age and weight. The average age of feedlot calves diagnosed with BRD is 202 d ± 51 d and ranged from 109 to 522 d (Snowder et. al., 2006). Some breed associations with age of greatest BRD morbidity has been noted; Limousin and Simmental expressed the youngest ages of diagnosed morbidity (190 d of age) and Charolais trended to be the oldest (213 d of age). The DOF when BRD was detected across breeds were 43 d, ranging by breed from 35 to 56 DOF, for Angus and Braunvieh, respectively (Snowder et. al., 2006).

Increased arrival weight, which typically indicates an older animal, results in decreased morbidity and culling risk while resulting in increased ADG and HCW (Babcock et al., 2013; Cernicchiaro et. al., 2013; Taylor et. al., 2010). Calves weighing less than average were 1.4 times more likely to be diagnosed with BRD (Gummow, 2000). Lightweight steers had increased morbidity risk during the spring and summer months: March to April, June to July, and October to November (Babcock et al., 2013). Mid-weight calves were most at risk for BRD morbidity during May to June (Babcock et al., 2013). Lighter BW female cohorts displayed a similar morbidity pattern, with lightweight heifers demonstrating increased risks in March and May and mid-weight calves had an increased risk in March to September (Babcock et al., 2013). This benefit of additional weight at the time of arrival may be a consequence of preconditioning programs implemented before arrival (Taylor et. al., 2010). However, a clear association between decreased morbidity rates with increased arrival weight has yet to be established (Taylor et. al., 2010).

Environment

The ability of the host to resist BRD is greatly impacted by the environment in which the interaction is made, affected by climate, ambient temperatures, change in temperatures, temperature extremes, wind, dust, and humidity with the largest incidence occurring around the time of the largest decrease in ambient temperature (Babcock et al., 2013; Snowder et. al., 2006; Cusack et. al., 2003). Another study suggested that the minimum temperature had a greater impact on BRD morbidity than the mean or the range and also suggested that extreme weather may just amplify the presence of the signs displayed by the host (Babcock et. al., 2013; Taylor et. al., 2010). Differences in morbidity rates could also be associated with the different management practices throughout the different seasons (Babcock et al., 2013).

Trends have been established between cattle arrival weight and arrival month with the greatest incidence occurring in late summer to mid fall through early winter. This occurrence is possibly due to the increased probability that lightweight, newly weaned, high risk calves will arrive at a feedlot during this time period due to traditional marketing timing (Babcock et al., 2013; Cusack et. al., 2003; Loneragan et. al., 2001). As a result, there is a larger population of disease organisms at locations during transportation where high densities of cattle populations are congregated (Taylor et. al., 2010). For instance, 17.3 of 1,000 died from BRD in December compared to 3.5 animals out of 1,000 deaths that were recorded in May (Loneragan et. al., 2001). Other research suggests that the risk for developing BRD is increased in the spring and summer months and that the severity of weather extremes and change in ambient temperature does not have a direct impact on BRD incidence rate (Babcock et. al., 2013; Taylor et. al., 2010). This is best described by Loneragan et al. (2001), as BRD incidence having two peaks, the first in spring and a second, larger peak occurring in late summer and fall.

Regardless, the magnitude of the economic impact as it pertained to the season of arrival was greatly affected by the number of treatments administered to the animal (Cernicchiaro et. al., 2013). Increased returns have been observed for cattle arriving in the summer and fall opposed to cattle arriving in the winter and spring with the expected returns decreasing at an increasing rate as the number of treatments increased. In cattle that were treated once or not at all, ADG was greater for spring and winter arrivals but HCW was greater in cattle received in the fall (Cernicchiaro et. al., 2013).

Time from arrival

The time span after arrival is also an important consideration for BRD management. An increase in incidence rate in 18,112 calves over 15 yrs has been observed after d 5 and incidence rate peaked around d 14 and remained increased until d 80 (Snowder et. al., 2006). Another study evaluating 1,519 pre-weaned calves and 3,277 head of feedlot cattle concluded that the d to first treatment average 40 d after arrival and 75% receive treatment by d 55 (Schneider et. al., 2009). Most animals that die from BRD do so in the first 2 months with a mean 48.6 d after arrival (Loneragan et. al., 2001).

A retrospective multivariable assessment combining morbidity and culling rates and the associated risk factors, using the collective data from 8,904,965 cattle and 54,416 cohorts, from 16 commercial U.S. feedlots were analyzed with a mixed effect multivariable negative binomial regression (Babcock et al., 2013). It was determined that the interactions between arrival weight, gender, and month of arrival were significantly associated with morbidity and mortality rates. This data set indicated that as arrival weight increased the associated disease risk decreased, but this was greatly impacted by gender of the animal. A seasonal association was also determined with increased risk for light and mid-weight calves arriving from March through September opposed to cattle arriving in November through February. It was reported that an increased evaluation of multivariable approaches were necessary when determining associated risk in heterogeneous cattle herds (Babcock et al., 2013).

Viral Respiratory Pathogens

Foreign microorganisms and pathogens initiate a response in host defense mechanisms resulting in a rapid inflammatory response (Godson, 1996). On the contrary, many healthy cattle carry one or more infectious viral and/or bacterial agents in the upper respiratory tract (Bagley, 1997). Some agents yield only mild clinical presentation; BRD is frequently a result of the interaction between a combination of viral and bacterial pathogens and stress (Muggli-Crockett et. al., 2013; Duff et. al., 2007; Cusack et. al., 2003). The viral infection predisposes the animal to bacterial infections by altering respiratory clearance mechanisms, damaging the lung and suppressing the host’s immune system (Muggli-Crockett et. al., 2013; Cusack et. al., 2003; Bagley, 1997).

Parainfluenza-3 virus

Parainfluenza-3 virus (PI-3V), of the paramyxovirus family, is usually associated with subclinical infection that leads to a secondary infection or specific proliferative giant cell pneumonia in young calves when combined with bacterial agents (Kahn et. al., 2005; Cusack et. al., 2003; Bagley, 1997; Lillie, 1974). The secondary infection occurs as a result of decreased immune and pulmonary defense mechanisms and suboptimal mucociliary escalator function (Cusack et. al., 2003). Acute PI-3V replicates in the epithelial cells in the upper and lower respiratory tract affecting alveolar macrophages and causing proliferation and necrosis of bronchiolar epithelial cells while destroying cilia in the bronchi. Furthermore, PI-3V infection compromises the lower respiratory tract resulting in bronchitis, bronchiolitis, and alveolitis (Cusack et. al., 2003).

Bovine respiratory syncytial virus

Bovine respiratory syncytial virus (BRSV), a pneumovirus in the paramyxovirus family, and characteristically forms syncytial cells in young, weaned, feedlot calves (Kahn et. al., 2005; Bagley, 1997). Bovine respiratory syncytial virus is important in the BRD complex as it destroys the ciliated respiratory epithelium and it affects alveolar macrophages by depressing cellular immunity in the lower respiratory tract, allowing for a pathway for a secondary infection (Kahn et. al., 2005; Cusack et. al., 2003).

Infectious bovine rhinotracheitis virus

Infectious bovine rhinotracheitis virus (IBRV), causes lesions, as a result of destruction of the epithelium with inflammation in the upper respiratory tract and trachea resulting in cessation of ciliary activity, decreased function of the mucociliary escalator, and a resulting failure to excrete particulate from lungs predisposing cattle to secondary pneumonia (Kahn et. al., 2005; Bagley, 1997; Yates et. al., 1982). Bronchoconstriction in the lower airways and immunosuppression, especially in the pulmonary defense mechanism, resulting in reduced neutrophil migration, cell mediated cytotoxity, mitogen responses of peripheral blood leukocytes, and some functional activities of alveolar macrophages, which also allows bacterial growth that manifests as secondary infection (Cusack et. al., 2003; Bagley, 1997). Many body processes are affected by IBRV including kidney, embryonic skin, adrenal, thymus, thyroid gland, pancreas, testicle, lung and lymph node but the respiratory system is the most commonly infected organ system in feedlot cattle (Kahn et. al., 2005; Yates et. al., 1982; Lillie, 1974). Infectious bovine rhinotracheitis virus is shed in nasal secretions that occur 12-14 d after infection and IBRV is capable of airborne transfer, especially during times of stress (Bagley, 1997; Yates et. al., 1982).

Bovine viral diarrhea virus

Bovine viral diarrhea virus is a highly infectious pestivirus in the flaviviridae family, and is the most frequently isolated viral agent (92%) in multiple viral infections in calves, suggesting that the presence of BVDV in a herd could be a primary pathogen involved in BRD pathogenesis (Richer et. al., 1988). Bovine viral diarrhea virus impairs the ability of the host to expel subsequent infection from the respiratory tract (Richer et. al., 1988) and is also an immunosuppressant affecting immune components of the respiratory system and other body systems resulting in diminished blood leukocytes and lung macrophage function allowing for a secondary infection of increased severity compared to the other isolated viruses, especially in the lower portion of the respiratory tract (Richeson et. al., 2012; Kahn et. al., 2005; Loneragan et. al., 2005). Other adverse effects like enteritits, abortion, and fetal malformation are also associated with BVDV (Loneragan et. al., 2005).

There are at least 2 different RNA genotypes and 2 antigenic differences: types 1a, Singer strain (BVDV1a), or 1b, TGAC strain (BVDV1b) and 2a, 125 strain (BVDV2), with BVDV type 1b being the most frequently isolated in the field (Richeson et. al., 2012; Duff et. al., 2007; Fulton et. al., 2006; Ridpath, 2005; Fulton et. al., 2000). The BVDV virus can also be characterized as either cytopathic or non-cytopathic based on the presentation and activity express in cultured epithelial cells (Ridpath, 2005). Biotype and genotype both have an impact on immune response, and both should be considered when implementing vaccination strategies (Fulton et. al., 2006; Ridpath, 2005). Antigenic variation occurs between the two genotypes and this variation between strains could result in unsatisfactory cross-protection by vaccines and differentiation by trained personnel making diagnoses (Ridpath, 2005). Due to lack of clear evidence, the exact role of BVDV in the pathogenesis of BRD has yet to be determined (Cusack et. al., 2003; Richer et. al., 1988).

Typically expressed as a subclinical infection, BVDV impairs humoral antibody production of other specific agents, monocyte chemotaxis and myeloperoxidase antibacterial system in polymorphonuclear leukocytes facilitating fibrinonecrotic bronchopneumonia lesions followed by lymphoid depletion resulting in inflammation of the respiratory tract (Loneragan et. al., 2005; Cusack et. al., 2003). Transmission can be from a fetal infection or from post-natal, airborne or direct contact transmission, with prenatal infection resulting in calving problems such as abortions, still births, congenital malformations and persistently infected (PI) calves (Duff et. al., 2007; Fulton et. al., 2006). Persistently infected cattle develop when the susceptible dam is exposed to non-cytopathic BVDV between 42 to 125 d of gestation; PI calves are immunotolerant to the virus and shed BVDV for life (Fulton et. al., 2006). The PI calves are recognized as the most detrimental BVDV source due to the constant and copious shedding of virus (Richeson et. al., 2012; Fulton et. al., 2006; Loneragan et. al., 2005). Approximately, 70 to 100% of naïve cattle become infected after exposure to PI cattle (Fulton et. al., 2006). Despite the observed prevalence of PI cattle, being relatively low (0.30%), direct contact with PI calves increased BRD incidence rate by 43% due to a high level, continuous source of infection in newly received, commingled cattle (Richeson et. al., 2012; Fulton et. al., 2006; Loneragan et. al., 2005). It has been determined that 2.5% of dead cattle and 2.6% of chronic cattle are PI (Loneragan et. al., 2005).

Although short term exposure may result in slightly increased performance early in the feeding period, similar to a vaccine, the detrimental effects of long term exposure to the host's immunity may result in performance loss through increased susceptibility to other diseases and infections and thus impact health as well as increased treatment cost (Richeson et. al., 2012; Smith, 2010). The presence of a PI-BVDV calf does not affect overall ADG but does contribute to decreased ADG from d 8 to 42 as nutrients are preferentially utilized in the immune and homeostasis pathways as opposed to growth (Richeson et. al., 2012). Control of BRD, as contributed by BVDV appears to be improved by the removal of PI calves, thereby reducing the risk associated with shedding of BVDV to susceptible cattle (Fulton et. al., 2006).

One investigator determined the prevalence of BVDV in 120 stocker calves, ranging from 315 to 495 lbs, acquired from 3 sale barns in Tennessee and then transported to West Texas (Fulton et. al., 2000). Cattle were administered a modified-live BHV-1 vaccination on d 0 and remained on study for 5 weeks with blood serum collected and examined weekly. Lungs were observed for homogenates and inoculated for virus isolation (Fulton et. al., 2000). Overall, 87.5% of cattle were treated for BRD, 13.3% died during the study, and no PI calves were detected. Throughout the duration of the study, BVDV type 1 noncytopathic (NCP) strains were isolated from 4 animals, PI-3V was isolated from 7 lungs, NCP BVDV type 1 from 1 lung, and 1 lung possessed both BVHV-1 and BVDV with *Pasteurella haemolytica* serotype 1 being the most frequently isolated bacteria (Fulton et. al., 2000). On d 34, 38.5% were positive for BVDV type 1, 27.9% were positive for BVDV type 2, 68.3% for PI-3V, and 77.9% for BRSV suggesting that BVDV type 1 cross reacts with BVDV type 2 and are intricately entwined with the infections of other pathogens that contribute to acute BRD. Fulton also reported that sale barn calves have an increased susceptibility to BHV-1, BVDV types 1 and 2, PI-3V, and BRSV early in the feeding period after entry into a feedlot (Fulton et. al., 2000).

Another study examined 11 natural BRD outbreaks in Quebec to categorize the antibodies of the viruses naturally found in the serum of animals (Richer et. al., 1988). Several viruses had concomitant outbreaks with other viruses, and fourfold concomitant of antibody titers were not uncommon; this was observed in 61% of young calves and 38% in mature animals. It was confirmed that BVDV was the most commonly isolated virus from calves with multiple viral infections (92%; Richer et. al., 1988).

An attempt was made to estimate PI prevalence and how it correlated with BRD morbidity outcome, chronically ill and dead PI cattle using 2,000 head of cattle at arrival, 1,383 hd of chronically ill cattle from 7 different feedlots, and 1,585 head of dead cattle (Loneragan et. al., 2005). Cattle were tested through immunohistochemistry to determine the prevalence of PI-BVDV positive cattle; health status was determined for both groups, exposed and not exposed. It was determined that PI prevalence for cattle on arrival, chronic cattle, and dead cattle was 0.30%, 2.60%, and 2.50%, respectively, with a 43% increase in the probability of treatment for BRD if cohorts were exposed to a PI positive animal. It was also concluded that 15.9% of initial BRD outbreaks were due to the presence of a PI animal (Loneragan et. al., 2005).

Another study investigated immunomodulation of cohorts exposed to PI cattle and how different management affected the effects of a PI animal prior to transfer (Richeson et. al., 2012). Different management groups included low risk, preconditioned calves or high risk, auction market cattle with or without exposure to a PI animal and data were analyzed from a 2 x 2 factorial arrangement of treatments. Preconditioned cattle were comprised of 236 head of cattle, averaging 251 kg from 3 different ranches; 292 head of cattle, averaging 245 kg were arranged from regional auction markets to comprise the high risk cattle. It was observed that ADG increased for the preconditioned cattle over the course of the study with a decrease of gain among the cattle exposed to a PI cohort (0.90 kg/d) compared to the control (1.12 kg/d) (Richeson et. al., 2012). It was also noted that morbidity decreased markedly for preconditioned ranch origin when compared to auction market cattle, 7 and 70%, respectively, with an increase in the rate of cattle requiring a third antimicrobial treatment and greater number of chronically ill cattle in the PI-exposed groups. This study determined that preconditioned calves experienced greater gains and less antimicrobial usage (Richeson et. al., 2012).

<u>Bacterial Respiratory Pathogens</u>

After a viral pathogen infects the host, opportunity for a secondary bacterial infection is enhanced. In order to understand the viral-bacterial synergism, the role of both the virus and the bacteria and the immune status of the host must be considered (Yates et. al., 1982). Bacterium establish in the lung causing pulmonary tissue damage with Lipopolysaccharide endotoxin in the outer membrane of Gram negative cell walls causing the recruitment of proinflammatory cells (Amrine et. al., 2014; Cusack et. al., 2003). Two or more microbiological agents, most commonly identified as *Pasteurella (Mannheimia) haemolytica, Pasteurella multocida* and *Histophilus somni (Haemophilus sommus), Mycoplasma bovis, arcanobacterium pyogenes, salmonella spp,* and *actinomyces pyogenes*, have been isolated from the upper respiratory tract in 40 to 60% of feedlot animals that died from BRD-related causes (Booker et. al., 2008). *M. haemolytica* serotype 1, followed by *P. multocida,* and *M. bovis* are the most commonly identified bacteria implicated in BRD (Amrine et. al., 2014; Lamm et. al., 2012; McClary et. al., 2011). Nevertheless, other species of bacteria may establish within a host if the opportunity arises (Cusack et. al., 2003). Trends in interactions have suggested that *M. haemolytica* typically interacts with BVDV and inhibits interactions with *H. somni* (Booker et. al., 2008). It has also been observed that *H. somni* and *M. bovis* are generally cultured together (Booker et. al., 2008).

Mannheimia haemolytica

M. haemolytica is the most commonly isolated bacterium from the lung of an animal diagnosed with BRD and from the upper respiratory tract in healthy calves (Amrine et. al., 2014; Lamm et. al., 2012; McClary et. al., 2011). Recognized for peracute, acute, and subacute infections, *M. haemolytica* is described as a right side bronchopneumonia causative agent unable to cause severe inflammatory reactions for more than a couple d (Amrine et. al., 2014; Hanzlicek, 2010; Booker et. al., 2008). *M. haemolytica* is also responsible for hemorrhage, increased fibrinogen in plasma, lysis of leukocytes and platelets, production of a specific leukotoxin that impairs phagocytosis, kills macrophages, and otherwise impairs the lungs natural defenses (Amrine et. al., 2014; Nikunen et. al., 2013; Cusack et. al., 2003). During high stress periods in the host, *M. haemolytica* rapidly multiplies in the upper respiratory tract and is transferred by nasal secretions allowing the bacteria to penetrate deeper into the lung resulting in fibrinous bronchopneumonia associated with BRD in the lower respiratory tract (Amrine et. al., 2014; Derosa et. al., 2000; Whiteley et. al., 1992). However, a detailed comprehension of interactions between the host and the bacteria is not well understood and involves additional factors for BRD to establish in the host; *M. haemolytica* is a commensal inhabitant of the upper respiratory tract in healthy calves (McClary et. al., 2011; Whiteley et. al., 1992; Yates et. al., 1982).

Fourteen auction market, crossbred steers were challenged with *M. haemolytica* to determine if clinical conditions including physiological, behavioral and pathological variables, were adequate indicators of BRD (Hanzlicek, 2010). Cattle were necropsied on d 1, 2, or 9 after being challenged. Physical measurements (temperature, heart rate, respiratory score, clinical illness score, and activity) were recorded 3 times daily, 4 d prior to inoculation, and continued through euthanasia subsequent to challenge to determine pathology. Although all animals were diagnosed with BRD after the challenge and demonstrated clinical signs, no clear indicator or BRD progression was identified. However, activity as measured with pedometers and accelerometers, decreased after inoculation and could serve as an early detection tool (Hanzlicek, 2010).

Another investigator defined the infectious pathogens, pathological processes, and interactions between the pathogens and the pathological processes associated with BRD (Booker et. al., 2008). Using 90 calves positively diagnosed with clinical BRD at the time of necropsy and 9 healthy animals as controls, various tissues were analyzed with immunohistochemical staining to determine pathogen prevalence. It was reported that *M. haemolytica* and *M. bovis* were the most commonly identified pathogens involved in fatal BRD necropsies. Significant associations included 96% of cattle positive for BVDV were also infected with *M. haemolytica*. Likewise, 80% of animals that were positive for *H. somni* were simultaneously positive with *M. bovis.* This study also noted that animals, positive for *H. somni,* were negative for BVDV and *M. haemolytica* (Booker et. al., 2008).

Pasteurella multocida

Pasteurella multocida is one of the bacterial pathogens commonly isolated from feedlot cattle and is linked to neonatal calf pneumonia (enzootic) and shipping fever when combined with a viral pathogen under times of stress (Dabo et. al., 2008; Cusack et. al., 2003; Bagley, 1997). The BRD morbidity rate in feedlot cattle attributed to *P.*

multocida is increasing and a strong connection has been established with its presence in clinical BRD of calves (Nikunen et. al., 2013, Dabo et. al., 2008). A gram negative pathogenic bacterium, *P. multocida* is typically cultured from bronchoalveolar lavage (BAL) and lavage fluid. *Pasteurella multocida* colonizes in the nares, nasal pharynx trachea, or bronchioles in calves (Nikunen et. al., 2013; Dabo et. al., 2008). *Pasteurella multocida* expresses general BRD signs and elevated concentrations of acute phase proteins, haptoglobin, serum amyloid A protein, and alpha acid glycoprotein; necrotizing pulmonary lesions have also been observed (Nikunen et. al., 2013; McClary et. al., 2011). Like *M. haemolytica, P. multocida* is identified in both sick and healthy calves, thus, the presence of *P. multocida* neither indicates nor predicts BRD (Dabo et. al., 2008).

A retrospective study compared treatment protocols of 43 necropsied cattle based on the antimicrobial susceptibility of the microorganisms cultured from the lungs; 16 were diagnosed with acute bronchopneumonia, 5 with subacute BRD, and 22 that were determined to be chronic cases at the time of post mortem evaluation (Lamm et. al., 2012). Forty lungs were cultured aerobically and 34 of them were positive for *Mycoplasma* spp. Thirty-nine lungs contained at least one bacterial pathogen as determined by lung culture, and 30 animals possessed multiple bacterial pathogens. Of the cattle cultured, 25 animals were positive for mycoplasma infection and 24 demonstrated complex infections with other bacteria (Lamm et. al., 2012). It was determined that 60% of the bacteria cultured (*M. haemolytica, P. multocida, and H. Somni*) were resistant to tetracycline. *Histophilus somni* demonstrated susceptibility (67% of cultures) to tilmicosin, enrofloxacin, ceftiofur, and florfenicol; whereas, *M. haemolytica* and *P. multocida* (65 and 79% susceptible isolates, respectively), were only susceptible to enrofloxacin and ceftiofur despite treatment antemortem. Investigators concluded that BRD-associated death of feedlot cattle is likely influenced by factors other than antimicrobial resistance (Lamm et. al., 2012).

Current prevention, treatment and control mechanisms

In an attempt to prevent, treat, and control BRD in cattle, feedlots must utilize different management practices, genetic improvements, and advancements in immunology, pathology, microbiology, and virology (Muggli-Crockett et. al., 2013; Berry et. al., 2011; Lillie, 1974). Timely, accurate, and effective diagnostic methods are the most critical control mechanisms (Moya et. al., 2015; Wolfger et. al., 2015; Szyszka et. al., 2012).

Vaccinations

Currently, the most effective preventative method related to infectious agents involved in BRD is modified-live or live-attenuated virus vaccines against the 4 major respiratory-associated viruses. Vaccinations have been shown to reduce carriage and shedding of infectious agents and create herd-level resistance (Snowder et. al., 2006; Fulton et. al., 2000; Bagley, 1997). Over 90% of large feedlots throughout the U.S. currently vaccinate cattle upon arrival against BVDV and IBRV, with the probability of an animal being vaccinated increasing as the capacity of the feedlot increases (USDA, 2013). Approximately 95% of large feedlots vaccinated against BVDV, 93.2% against IBRV 89.5% against BRSV, 81.3 to 85.1% against PI3V, 84.4% against clostridial diseases, 69.7% against *H. somni* and 63.8% against "*Pasturella"* (USDA, 2013; Godson, 1996). Nevertheless, a single commercial vaccine containing agents intended to protect against all of the potential pathogens is unavailable (Muggli-Crockett et. al., 2013). About one-half of U.S. feedlots alter vaccination protocols according to the demographics of the group of cattle being processed, especially in cases where high risk calves were involved (Amrine et. al., 2014; USDA, 2013; Kasimanickam, 2010).

Vaccinations are directed predominately at the viral pathogens (USDA, 2013). Antimicrobials used to treat secondary bacterial infections have indicated positive results on health and performance outcomes in the feedlot (Amrine et. al., 2014; McClary et. al., 2011; Bagley, 1997). Anti-inflammatory drugs have been indicated to be beneficial to reduce fever and lung damage as well as enhance convalescence (Kasimanickam, 2010; Cusack et. al., 2003). Vaccinations are clearly efficacious when administered in advance of homologous pathogen challenge, but little data supports efficacy to control or treat BRD and no effective viral treatment has been identified (McGuirk, 2014; Lamm et. al., 2012; Richeson et. al., 2008).

Diagnostic methods

As BRD is the most recognized disease affecting feedlot cattle, implications with current identification systems arise due to a lack of specific diagnostic methods (Tennant et. al., 2014; Duff et. al., 2007). Inability of the health technician to make accurate diagnoses is influenced due to the nature that cattle, being prey animals, possess the instinct to disguise illness and vulnerability from perceived predators (McGuirk, 2014; Tennant et. al., 2014; Duff et. al., 2007; Snowder et. al., 2006). This is the foundation behind potential BRD predictive variables used to better diagnose disease and refine metaphylactic treatment. Both extremes of cattle affected with BRD have the potential not to be treated; if the animal is too severely ill due or if the animal is suffering from a mild, or subclinical case of BRD, the animal is less likely to receive treatment (USDA, 2013). Subjective visual appraisal based on a combination of clinical signs is the predominant method of disease detection in the feedlot and occasionally the decision to provide antimicrobial treatment is influenced by the status of febrile condition (> 104°F rectal temperature). However, this method may be a poor assessment of an animal's health as rectal temperature can vary in response to other conditions such as time of d, environment, and handling (Moya et. al., 2015; McGuirk, 2014). Unfortunately, morbidity rates as related to BRD have not decreased, but rather have increased in the last 20 yrs. Data from 1994, 1999, and 2011 indicate an increased rate of 10.3, 14.2, and 16.0%, respectively, per thousand hd on feed (Hilton, 2014).

There is great need for a reliable, accurate, repeatable, and cost effective diagnostic method for BRD before consistent diagnoses can be established (Moya et. al., 2015; Tennant et. al., 2014; Buckham et. al., 2007). Control of this disease can only be accomplished with increased understanding of the interactions between the host immune and respiratory systems, infective pathogens, and environment (Lillie, 1974). Economical, chute–side diagnostic tools would be beneficial and have been suggested as a possible treatment decision tool in the commercial setting (Duff et. al., 2007). Diagnostic tools could consist of pedometers, feed or water intake monitors, continuous body temperature monitoring devices, electronic stethoscopes, and ultrasound equipment (McGuirk, 2014). Control can only be obtained if pathogen exposure and transmission between cattle and a possible epidemic outbreak is reduced (Snowder et. al., 2006). Considerations towards methods of challenging cattle with BRD pathogens in a controlled manner that is inexpensive and humane would be an important advancement to better understand the interactions (Snowder et. al., 2006).

Management practices

Management of BRD is related to both the animal as well as different pathogens associated with the disease (Tennant et. al., 2014). Some current management practices that have been demonstrated to be effective in BRD control include preconditioning, metaphylaxis, and the attempt to reduce the number of stressors presented to the animal simultaneously (Schneider et. al., 2010; Cusack et. al., 2003; Bagley, 1997). Sick animals in the feedlot would benefit from early disease detection and treatment (Hilton, 2014; Hanzlicek, 2010; Kasimanickam, 2010; Bagley, 1997). Care should be taken to reduce known stressors by carefully selecting the timing of processing and handling, understanding the demographics of the herd, and developing an awareness of critical periods for BRD occurrence (Babcock et al., 2013; Hanzlicek, 2010; Smith, 2010; Cusack et. al., 2003). A working relationship between licensed veterinarians, nutritionists, and facility managers should be established to create vaccination and health management protocols (McGuirk, 2014; Kasimanickam, 2010; Duff et. al., 2007). Other mitigation strategies include pre-weaning management including preconditioning practices such as vaccination, castration, weaning, bunk training and proper nutrition (Kasimanickam, 2010).

Preconditioning

One such prevention strategy is preconditioning calves before arrival to the stocker or feedlot using a pre-transport preventive health program. This practice has been shown to reduce morbidity and mortality by decreasing the number and intensity of stressors associated with relocation from the ranch origin to the feedlot (Hilton, 2014; Richeson et. al., 2012; Hilton et. al., 2011). A sound preconditioning program allows calves to have been weaned 30 to 45 d before transport, with vaccination, castration, anthelmintic treatment, dehorning, and exposure to feed bunks before the cattle arrive at the feedlot (Hilton, 2014; Richeson et. al., 2012; Hilton et. al., 2011; Kasimanickam, 2010; Step et. al., 2008).

It has been suggested that preconditioning does not necessarily reduce BRD cases, but rather disperses the clinical signs and the effects of morbidity into a more manageable spectrum; the benefits of preconditioning are reduced if cattle are commingled during transport or upon arrival (Hilton, 2014; Taylor et. al., 2010). Preconditioning programs are not widely adopted in the cow calf segment and must be evaluated in different production systems for economic and production benefits unique to the operation. Preconditioning increases selling weight of weaned calves, which results in an estimated economic impact of 63%; there is some added profitability due to price advantages but added return is dependent on the marketing basis (Hilton et. al., 2011). Preconditioning may improve performance and decrease COG over time, but profitability is impacted by several factors (Hilton et. al., 2011).

Another study was conducted to compare different production and carcass characteristics and economic value between 600 head of cattle divided into 3 groups: those with unknown health history, weaned for 45 d prior to transport, and weaned and vaccinated 45 d prior to transport (Seeger et al., 2008). Animals of unknown medical history before arrival to the feedlot were more likely to exhibit clinical signs of BRD, were treated more frequently, and died more often than cattle that underwent preconditioning protocols before arrival. Signs of BRD typically appeared in an animal with unknown histories earlier in the feeding period compared to preconditioned cohorts. It was concluded that cattle with unknown health history have an increased probability of being diagnosed with BRD in the first 28 d after arrival (Seeger et. al., 2008). Furthermore, cattle of unknown health origin took longer to finish with increased DOF, decreased ADG through the feeding period, and consumed less total feed on a daily basis resulting in slower gain. However, this slower gain and decreased feed intake resulted in similar G:F between the management groups, and total COG was less for cattle of unknown health history (Seeger et. al., 2008).

Overall, the cattle with unknown health background resulted in less net profit over the entire feeding period. Preconditioned calves with known backgrounds typically have improved gains with similar G:F compared to cattle of unknown health history as a result of improved overall health and reduced subclinical illness. However, due to the less expensive purchase cost of cattle with unknown health origins, high risk cattle are competitive cattle in the market and oftentimes do not yield a substantial difference in net returns upon harvest (Seeger et. al., 2008).

A study was conducted to determine profitability and necessary factors of utilizing a preconditioning management plan in a commercial beef herd (Hilton et. al., 2011). Average returns of $80.70 per calf with a range of $26.04 to $116.48 per calf were reported and profitability increased as the manager gained experience with the preconditioning program. Nevertheless, seller profits were realized during every yr of the study; additional profits achieved with preconditioning of weaned calves were attributed to additional weight gain or health sales price advantage (Hilton, et. al., 2011).

Metaphylaxis

Another common, cost effective management practice used to effectively reduce BRD incidence in high risk calves is metaphylaxis, defined as mass treatment with parenteral antimicrobials at the time of arrival to a stocker or feedlot facility (Tennant et. al., 2014; Cusack et. al., 2003; Lofgreen, 1983). Administration of antimicrobials to control BRD in high risk calves is commonplace in the beef industry and has been shown to reduce the mean number of treatment d and reduce morbidity rate as well as improve feed intake and gain (Tennant et. al., 2014; Smith, 2010; Duff et. al., 2007).

Considerations to the demographics of a group of cattle and the weather conditions at arrival are important in the management decision to use metaphylactic treatment of calves upon arrival (Moya et. al., 2015; Cernicchiaro et. al., 2013; Kasimanickam, 2010; Taylor et. al., 2010). In lightweight or naïve calves, metaphylaxis has been consistently documented to have efficacy and a justifiable economic investment but as weight of calves on arrival increases, the efficacy of the procedure is likely to decrease (Tennant et. al., 2014). Nevertheless, current metaphylaxis protocols are administered to entire groups of cattle based on factors such as perceived stress level, age, degree of commingling, source of acquisition such as an auction market, transport distance, and weather conditions. It is plausible that the conditions of relocation also increase the risk of exposure to respiratory pathogens. Various factors are likely to influence treatment costs, decrease performance, and overall value (Moya et. al., 2015). Due to potential antimicrobial resistance and social pressures associated with metaphylaxis, alternative disease control methods, or methods to refine metaphylactic treatment such as utilizing complete blood count or other blood variables seems warranted. In one study, cattle with low eosinophil and high red blood cell concentration were at greater risk for clinical BRD and these methods could be investigated to better target metaphylactic treatment decisions (Richeson et. al., 2013).

The efficacy of metaphylaxis to reduce pulmonary lesions after cattle were inoculated with *M. haemolytica* was recently evaluated (Amrine et al., 2014). Investigators assigned 33 head to 1 of 3 treatments consisting of tildipirosin (Zuprevo), tulathromycin (Draxxin), or a saline control and intratracheally administered *M. haemolytica* challenge on d 10 post-challenge. Animals were monitored and observations in clinical illness scores (CIS), injection site reactions, respiration quality scores, rectal temperature, and appetite scores through d 13 were recorded. The percentage of the affected lung, post-challenge, ranged from 3.3 to 39.8%. Tildipirosin effectively reduced the presence of lesions when compared to the other 2 treatments, with 92% yielding an observed rate of <10% lesions; tildipirosin also improved CIS scores, respiratory scores, and appetite scores. This study suggests that tildipirosin results in fewer clinical signs of illness and less lung damage when compared to tulathromycin or saline control (Amrine et. al., 2014).

The results of metaphylactic treatment on performance, presence of lung lesions at slaughter, and the association between lung lesions and performance in 2,366 head of commercial cattle at a feedlot in the Texas Panhandle were determined (Tennant et. al., 2014). Cattle administered tilmicosin (TIL) were eligible for BRD treatment after a 3 d post-metaphylactic interval (PMI), whereas, the PMI for tulathromycin (TUL) was established as 10 d. Metaphylatic treatment with either drug resulted in a difference in final BW, HCW, back fat, and dressed yield when compared to steers that were not administered metaphylaxis. However, no differences were observed for G:F and DMI; only ADG was improved in the metaphylactically treated groups (Tennant et. al., 2014). Furthermore, no differences were detected in LM area, marbling, or calculated yield grade. Decreases in BRD morbidity as well as overall morbidity were observed for the TUL treatment. No differences were observed concerning lung lesions across all treatments (Tennant et. al., 2014).

As a result, economic losses are directly related to reduced ADG and increased mortalities in cattle that did not receive metaphylaxis and additional medical costs in the groups that were treated, with TIL being the lesser overall cost of the two metaphylactic treatments evaluated (Tennant et. al., 2014). It was determined that metaphylaxis is an effective risk management tool used to reduce the number of cattle with clinical BRD. Groups that returned increased gross revenue were the groups that were treated with TUL and TIL, respectively (Tennant et. al., 2014). Overall, the presence of lung lesions at slaughter was associated with a decrease in HCW and kidney, pelvic and heart fat (KPH). The 15CON (5-15% Consolidation of tissue or mycoplasma-like lesion), 50CON (15-50% consolidation of tissue, pleural adhesion, or percent lung missing), and ALLCON (greater than 50% consolidation of tissue, pleural adhesion, or missing lung) lung score categories were associated with a decrease in back fat, marbling, calculated yield grade and empty body fat. Interestingly, there was no difference in LM area for the 15CON and 50CON categories, only the ALLCON was observed to possess a reduction in LM area. Overall, there was no difference in quality or yield grade distribution, but there was a decrease in gross revenue across all severities of lung lesions. Thus, all of the carcass factors resulting in decreased performance were indicated by reduced HCW, KPH, back fat, marbling, calculated yield grade, and empty body fat, all directly associated with fat composition (Tennant et. al., 2014).

Disease Parameters

Biological Reasons for Activity Change

Activity or behavior is one of the first aspects of an animal affected by disease and is the most common parameter used in the diagnosis (Szyszka et. al., 2012). Changes in behavior such as anorexia, depression, lethargy, and reduction of grooming are typically indicators of the presence of disease caused by viral or bacterial infection when accompanied with a febrile response (Robert et. al., 2009; Urton et. al., 2005; Hart, 1988). Biological changes, centered on a febrile response, are likely a result of evolutionary selection a million yrs in the making. One scientist summarized the biological changes as an "organized, evolved behavioral strategy to facilitate the role of fever in combating viral and bacterial infection…in an all-out effort to overcome the disease, putting virtually all the animal's resources into killing off the invading pathogen" (Hart, 1988). The non-immunological disease fighting strategies represent an animal's first line of defense against foreign pathological infections before the immune system has time to fend of the infection.

"The acute phase response (APR) is defined as the body's early defense mechanism in response to trauma, inflammation or infection, and is facilitated by a cascade of systemic physiological reactions" (Hughes et. al., 2013). Activated leukocytes produce pro-inflammatory cytokines (i.e. tumor necrosis factor α (TNF-α), interleukin 1

(IL-1), interleukin 6 (IL-6), and interferon gamma (IFN-γ)) initiate changes in the target cells allowing for the cells to fight infection (Hughes, et. al., 2013). The APR leads to systematic responses including fever, leukocytosis and activation of complement and clotting systems, alteration in plasma concentration, and changes to the liver metabolism as well as the release of acute phase proteins (APP; Godson, 1996). Hepatic production of APP is accompanied by activity changes, fever, and metabolism adjustments (Hughes, et. al., 2013). This metabolism increase is recorded at 13% per degree Celsius (Dubois, 1948). As the APR response activate fever, which triggers a series of changes within the animal that decreases overall cattle activity.

Decreased movement results in less muscular activity, conserving energy for metabolic costs of the immune system to combat disease (Hart, 1988). The introduction of a fever yields a raised thermostatic setting resulting in an animal feeling cold at temperatures that were perceived as normal before the infection. To conserve body heat, blood is redirected to internal organs and muscle contractions to induce shivering are utilized to produce extra body heat. (Hart, 1988) As a result, cattle become hunched up or lay down in an attempt to conserve body heat. In addition, there are increased energy costs imposed on the body both by accelerating metabolic processes and by increasing the metabolism by way of shivering to maintain an elevated body temperature.

Anorexia is induced by pro-inflammatory cytokines such as IL-1 secreted by leukocytes during an acute phase response; their actions influence hypothalamic temperature regulation in the brain. Though perceived as a problem due to lack of caloric and protein intake, anorexia likely developed as a way to reduce iron intake. A decrease of iron in plasma levels when combined with a fever hinders viral and bacterial growth and is one of the components that trigger an immune response. Bacteria multiply with plasma iron from serum transferrin, a glycoprotein responsible for the transport of iron to areas of the body responsible for iron absorption, storage and utilization. Thus the loss of appetite could be perceived as a survival mechanism to maintain a fever and keep blood iron concentration at a minimum (Hart, 1988). Furthermore, when cattle minimize energy usage typically used for feed and water consumption, body energy reserves can be expended towards the increased metabolic costs of fever and immunological processes, while reducing heat loss.

Interestingly, IL-1 and anorexia has also been linked to increased lethargy which is tied to the conservation of energy needed for metabolic increases. Cattle will remain in a lying state to conserve both heath and energy (Hart, 1988). Furthermore, sleep is vital in the body's natural recovery mechanisms and this may be an adaptive, "last ditch survival" method, before exhausting cattle's resources. Lethargy could also potentially serve as a protection from predation as cattle's strength is compromised.

Reduced grooming is affected by lethargy, but is more likely associated with cattle's attempt to reduce heat loss from a decreased surface area exposed to air movement and decrease energy depletion. Additionally, increased grooming is associated with increased water loss through saliva. It has been calculated that approximately a third of nonevaporative water loss is achieved through grooming (Hart, 1988). As a result, reduced grooming will conserve water resulting in a decreased impact on the body by dehydration.

Pedometer Usage

Originally intended for military usage by Leonardo de Vinci to monitor and record number of steps, the first pedometers provided the primitive foresight and technology for modern pedometers The basic mechanical pedometer, patented in 1927 (Filed August 23, 1927: US 1685242 A), used a pendulum which contacted a post each time a movement was detected, recorded as a step (MacCurdy, 1938). Unfortunately, this technology was unable to decipher a step from other movements. With improvements and advancements in technology incorporated into pedometers, the first design introduced by de Vinci has evolved into an electronic monitoring device used in research to monitor and log activity (MacCurdy, 1938).

Current accelerometers record three dimensional movement that generate a change in electrical output voltage relative to duration of standing and lying time, number of steps taken, and duration of lying bouts allowing a detailed report on activity to be quantified and a proprietary motion index indicating overall activity using a proprietary algorithm (Robert et. al., 2009). A piezoelectric effect, incorporating a microscopic crystalline structure of quartz or ceramic crystals, is used to generate an electrical voltage when stressed which is sent to a processor chip capable of recording movement and posture. Differentiation between activity variables are determined by specific orientation of the device, attached to the leg, and the respect to the gravitational field; when cattle are in a standing position, "the full force of gravity is recoded on the X-axis while the Y-axis is in a nearly neutral position" and when then animal is lying down the axes are reversed (Robert et. al., 2009). This differentiation allows for clear data points for different postures (Robert et. al., 2009). Data is collected based on pre-defined recording intervals, epochs, and evaluated with pre-determined thresholds and algorithms (Robert et. al., 2009; Løvendahl et. al., 2008). Data is then transferred to external computer software via radio transmission or manually downloaded after removal and transposed in lying or standing postural orientations as well as walking and transition movements (Robert et. al., 2009). Accelerometers provide non-invasive, accurate, and objective measurement to quantify activity levels in cattle and could be critical in BRD diagnosis (Robert et. al., 2009; Roelofs et. al., 2005).

IceQube accelerometers (IceRobotics, Edinburgh, Scotland, UK), designed for both research and commercial use in livestock operations, are encased in a plastic band to allow ease of access and are intended for attachment to the rear leg of cattle for activity monitoring. Measuring 95.0 mm x 82.3 mm x 31.5 mm and weighing 130 g, the devices are capable of continuous monitoring of activity without imposing on or altering an animal's normal behavior and without providing discomfort to the animal. Data is recorded in 15 minute intervals and stores data for up to 60 d and is easily downloaded with an IceQube tag reader (Ice Robotics). IceQube accelerometers have been proven to be both accurate and effective methods for monitoring activity in cattle (Nielsen et al., 2010; Trénel et al., 2009; Endres et. al., 2007).

Regardless of the sensitive nature of behavioral changes to detect diseases, the producer is limited in the ability to monitor, interact, and detect disease due to the limitation of trained personnel in the workforce and the instinct to conceal weakness to a predator (Robert et. al., 2009; Muller et. al., 2003; Frost et. al., 1997) A remote activity monitor could aid both researchers and producers as technology improves and becomes more cost effective and user friendly (Robert et. al., 2009; Urton et. al., 2005).

Combining the strengths of clinical observations with a computer-based integrated activity monitoring system may improve timely disease detection and allow for comprehensive knowledge of behavioral activities while simultaneously improving animal husbandry practices and reducing health costs (Robert et. al., 2009; Frost et. al., 1997).

It would also be useful in detecting subclinical disease which by definition would escape current diagnostic methods due to lack of clinical signs or detecting disease before clinical signs became evident (Gonzalez et. al., 2008). Accelerometers that continuously record activity in cattle are gaining popularity due to easy application, and ability to detect quantity and intensity of activity variables. Importantly, accelerometers may serve as a manageable data collection tool without affecting animals' natural expression of behavior (Muller et. al., 2003). However, methods to monitor behavioral alterations in cattle as an early disease diagnostic tool need to be both sensitive and specific to warrant application in the commercial feedlot setting (Urton et. al., 2005).

A scientist validated the IceTag data sensor for recording activity while improving the system by incorporating a filtering procedure to dictate changes in posture (Trénel, et. al., 2009). Cutoff thresholds were determined that capitalized sensitivity and specificity, and an experiential lying period criterion (LPC) was established as a filter for IceTag. The thresholds were then applied to a new filter that categorized movement as upright movement. Total activity of 9 calves, 4 of which were used to determine an LPC and 5 of which were used for validation, were recorded by both pedometer and video and analyzed with a 2 × 2 contingency table. An optimal LPC was obtained by minimizing deviance between the pedometer data and the video data. It was observed that the IceTag can “accurately measure the high-prevalence behaviors (lying and standing; Se+Sp > 1.90) and less accurately measure low-prevalence behavior (moving; Se+Sp =1.39). An LPC of 24.8 s was determined to present the most optimal portrayal of cattle’s activity (Se+Sp =2.00, precision of 0 to 49s, 95% confidence interval). It was concluded that IceTags provide valid duration and quantification of activity periods (Trénel, et. al., 2009).

One study evaluated the potential for the IceTag data logger (IceTag Sensor, IceRobotics Ltd, Edinburgh, UK) to affect cattle’s natural expression of lying behavior (Gibbons et. al., 2012). Forty dairy cows were fitted with Ice Tag Sensors, and with a smaller data sensor to analyze duration of lying bouts, frequency, and the percentage of lying time per side. Of the 40 cows, 16 cows were split into 2 groups and collected data were analyzed with a Latin square design: no IceTag (6d), and an Ice tag on the right hind leg (6d), on the left hind leg (6d), and on both hind legs (6d). They reported that 39 of the cows spent 47.5% of the total time lying, on the right side with a range of 25.1% to 65.7%. No effect was noted for placement of the IceTag or for treatment. It was concluded that IceTags could be “reliably used in research…to measure activity” and that individual preference of the cow is the sole determinant of the side a cow lays on (Gibbons et. al., 2012).

Another study developed algorithms for standing and walking detection in dairy cows using accelerometers (Nielsen, et. al., 2010). After being fitted with an accelerometer on the rear leg, 10 cows were stimulated to stand for 20 seconds and then walk for a period of 10 seconds, sequentially for 10 minutes. Then the same cattle were encouraged to move the legs while standing. Video behavior recordings were analyzed on a per second basis for walking, standing behavior, and number of steps. It was concluded that number of steps over a given time and the frequency of standing and walking could be precisely assessed by the accelerometer (Nielsen, et. al., 2010).

Researchers used triaxial accelerometers to count steps and differentiate gaits in 7 dairy calves when compared to video recordings (de Passillé, et. al., 2010). Calves were asked to walk, gallop, or trot around an area; step count was recorded and analyzed with both the accelerometer and manually through visual recordings. It was noted that steps recorded between the accelerometer and the video recordings were highly correlated and that interpeak intervals could successfully distinguish between different gaits. Authors reported that automated measures of acceleration are practical to determine step count and gait (de Passillé, et. al., 2010).

Impact of Behavior on Health

One researcher, realizing the importance of behavior on animal's health and well-being, investigated the accuracy of accelerometers (GP1 SENSR units, Reference LLC Elkader, IA) to monitor and document cattle activity in 15 crossbred beef calves (Robert et. al., 2009). Classification trees were established based on agreement of accelerometer data with video analysis serving as the gold standard for behavior monitoring. It was discovered that lying and standing activity demonstrated superb agreement with the video with 99.2 and 98% accuracy, respectively, and good agreement on walking (step count) with a reported 67.8% accuracy. Investigators concluded that "accelerometers provided an accurate, remote measure of cattle behavior" (Robert et. al., 2009).

It was suggested that factors resulting in a chronic health conditions could induce gradual but persistent activity changes; whereas, changes in activity associated with acute health conditions are dependent on the type of challenge (Szyszka et. al., 2012). While change in activity, measured by total steps taken or duration of lying or standing, may indicate early BRD morbidity, as number of steps decrease after infection, but change in activity fails to correlate with the intensity of the disease (Szyszka et. al., 2012, Hanzlicek, 2010). Prior to infection, cattle spend a greater amount of time standing than lying down, and this activity is inverse 10 h after an animal has been infected, and may be associated with clinical depression (Szyszka et. al., 2012). It was noted that the most significant behavior changes after being exposed to a health challenge, was the duration of lying time increased and the frequency of lying bouts decreased when compared to healthy cohorts; alterations persisted for approximately 30 d post inoculation (Szyszka et. al., 2012). It was also observed that the overall standing or lying times did not differ between sick and healthy cattle, rather the amount of changes in activity decreased, resulting in an infected animal changing body position, such as lying bouts, less frequently (Szyszka et. al., 2012). Consequently, continuous monitoring of activity with accelerometers is a promising tool for novel disease detection, as infection affects activity and can assist in identifying sick animals earlier especially when coupled with other diagnostic methods (Wolfger et. al., 2015; Moya et. al., 2015; Szyszka et. al., 2012).

Additional research evaluated how changes in activity patterns, as corresponding with acute or chronic health challenges, could potentially develop into an efficacious disease detection tool and proposed that activity changes associated with chronic disease take longer time to advance but remain more persistent (Szyszka et. al., 2012). Holstein-

Friesian bulls were challenged at the time of processing with intravenous lipopolysaccharide (LPS) bolus for the acute challenge, the abomasal parasite *Ostertagia ostertagi* for the chronic challenge, and a control. To monitor activity and posture, accelerometers were attached to the front leg; eating and drinking behavior was monitored by video. It was determined that chronic challenged animals experienced reduced BW after d 17 with no difference between the acutely challenged animals and control (Szyszka et. al., 2012). Activity changes were first noted as a reduction in activity, demonstrated by decreased number of steps, approximately 10 h after the initial challenge for the acutely challenged bulls; chronically challenged bulls demonstrated a decrease in laying or standing frequency and increase in average lying time after d 19 (Szyszka et. al., 2012). The decreased activity in challenged animals remained for approximately 30 d after inoculation. Coupled with slightly increased duration of feeding bouts, activity changes, especially posture indicated by less frequent buy increased length of lying bouts, have the potential to serve as an indicator of disease, but it would be necessary to incorporate other detection factors in order to be a viable tool to the industry (Szyszka et. al., 2012).

One researcher evaluated the effectiveness of electronic activity measurement using an ALT-pedometer to evaluate changes in activity patterns incurred by lameness (Alsaaod, et. al., 2012). Data analyzed included lying time, lying bouts and duration for each activity. Locomotion was assign using a 5-point numerical rating system (NRS): NRS $\leq$2, NRS =3, NRS =3.5. Eleven lactating Holstein cows (NRC$\leq$2) with approximately the same amount of lameness were analyzed, resulting in 549-d dataset. It was observed that the variability may be greater in the individual animal than the change as a result of lameness, and pedometers may more beneficial if used for classification as opposed to prediction (Alsaaod, et. al., 2012). When evaluating the deviation of normal behavior, 76% accuracy was achieved opposed to that obtained with the use of absolute values (65%). It was suggested that a model incorporating multiple aspects of lameness would be more beneficial and that using a pedometer in combination with machine learning tools could accurately detect lameness (Alsaaod, et. al., 2012).

Another study analyzed the use of pedometers to detect lameness earlier then able to be achieved by visual appraisal (Mazrier, et. al., 2006). Technology was programmed to alert trained animal caregivers of a 5% reduction in activity compared to the previous 10 d average; animals were then evaluated for clinical lameness. Furthermore, data from animals detected for lameness through visual detection was consulted to determine the time, duration, and quantity of activity reduction. Of 400 Israeli-Holstein cows observed, reduced activity was observed in 46 hd and 38 cows expressed lameness. Of the 38 head expressing lameness, 45.7% (21 head) were detected 7 to 10 d prior to visual appraisal with the 5% threshold. When lameness was detected with the reduction of activity, 92% expressed changes in activity of upward of 15% (Mazrier, et. al., 2006).

One study utilized accelerometers to detect differences in behavior before and after castration (White, et. al., 2008). The study placed 2 dimensional accelerometers on 3 healthy Holstein calves and compared with video observation to validate the algorithms in the model. Accelerometers accurately detected posture (98.3%) and specific activity (23.5% misclassification rate). Then 6 head of castrated beef calves and 6 head of non-castrated bull controls were then compared using the previously validated algorithms. It was determined that castrated beef calves spent a greater amount of time standing opposed to steers that were not castrated, 82.2 and 46.2%, respectively.

Impact of Behavior on Estrus

Monitoring of behavior with electronic activity tags, accelerometers, or pedometers have been utilized by the dairy industry to indicate the onset of estrus (Saint-Dizier et. al., 2012; Løvendahl et. al., 2008; Roelofs et. al., 2005). After activity increased, indicating estrus periods in cattle, researchers have indicated that ovulation occurs 29 h after a rise in activity (Saint-Dizier et. al., 2012; Roelofs et. al., 2005).

In a study evaluating the relationship between activities surrounding estrus and time of ovulation to determine if activity is an acceptable indicator of ovulation, 43 Holstein-Friesian cows were observed for a combined 63 ovulations and signs of estrus were physically observed in 3 h intervals (Roelofs et. al., 2005). Data were analyzed in 2 hr time periods by pedometers and defined using predetermined algorithms and thresholds. Behavioral estrus over all cycles was detected 51 to 87% of the time and estrus periods, determined by more than one animal being in estrus, were detected 95% of the time. Increased number of steps were observed during the estrous period and increased as the number of cows entered behavioral estrus and steps were also increased in primiparous heifers compared to multiparous cows. It was determined that ovulation occurred 29.3 ± 3.9 h after activity increased (39 to 22 h prior) and 19.4 ± 4.4 h after this period of increased activity ended (around 35 to 12 h). This study concluded that pedometers accurately identify estrus in dairy cows and could be a promising diagnostics tool to improve timing of fertilization and pregnancy percentage (Roelofs et. al., 2005).

A similar study compared duration of increased activity and intensity of activity as a decision making tool to determine estrus in dairy cattle (Koelsch et. al., 1993). This study collected activity data using activity monitors, in 1-min intervals, to determine the use of activity. Activity monitors were placed around the neck on 21 Holstein cows ranging from 10 to 60 d post-partum and collected 41 estrus periods over a span of 600 d. Pedometers were attached to the rear leg 6 cows to provide comparative data. A temporal activity pattern was identified for both estrus and dioestrus periods, however a more significant behavior change was observed during estrus. Activity monitors, when coupled with other indicators of estrus, can more accurately predict behavioral estrus and pre-ovulatory spike of luteinizing hormone (Koelsch et. al., 1993).

Electronic activity tags or pedometers were also reported to aid in estrus detection and estrus intensity in a more recent study (Løvendahl et. al., 2008). The study included 211 Holstein cows, 178 Red Dane cows, 126 Jersey cows, and 132 heifers. It was determined that activity episodes, defined as the amount of time from which one activity begins to the time it ends, indicating the start of a new activity, lasted 9.24 h in relation to estrus in primiparous heifers compared to 8.12 h in multiparous cows with Red Dane cows having a reduced time prior to increased activity and Jerseys having a reduced duration of activity in relation to estrus. It can be determined that activity monitors are capable of providing valuable information on management of fertility in dairy herds (Løvendahl et. al., 2008).

Feeding Behavior

Feeding behavior is also a very valuable tool for disease detection and has been used in both dairy cattle and beef cattle (Gonzalez et. al., 2008; Urton et. al., 2005).

Researchers have found that time spent feeding decreased an average of 35% over 4 d for cattle diagnosed with BRD; decreased numbers of meals were also observed in cattle with BRD (Urton et. al., 2005). Depressed feeding behavior is capable of recognizing morbidity 4.5 d earlier than trained health personnel monitoring clinical signs of BRD (Urton et. al., 2005). By utilizing feeding behavior, 80% of cattle with acute diseases were detected 1 d prior to identification by feedlot personnel, with short term changes in feeding behavior being indicative of the onset of health disorders (Gonzalez et. al., 2008).

In a study to improve recognition of metritis with recognition of changes in feeding behavior as associated with metritis risk, 26 Holstein cows were monitored 2 weeks before calving through 3 weeks post calving (Urton et. al., 2005). Investigators determined that only 69% of afflicted animals showed clinical signs of metritis as defined by increased rectal temperature and vaginal discharge and cows spent an average of 22 min less per d in the feed alley when compared to healthy cows. It was noted that as time at the bunk decreased by 10 min, the risk for metritis diagnosis increased two-fold. Investigators concluded that decreased feeding behavior can be a tool to help assist with early diagnosis of health related issues and diseases or metabolic disorders (Urton et. al., 2005).

In a retrospective study, investigators evaluated changes in short term feeding behavior and its association with common health problems in the dairy industry, ketosis, acute locomotor problems, and lameness in an attempt to quantify changes in behavior and the ability for behavior changes to serve as a potential early indicator of disease (Gonzalez et. al., 2008). Ketosis was identified in 8 dairy cows and decreased intake, feeding time, and feeding rate were observed in the affected cows. Fourteen cattle demonstrated acute locomotion disorders and also demonstrated decreased feed intake and feeding duration, though an increase in feeding rate was observed. Lame cows were also reported to have decreased feeding times, feeding frequencies, and feeding rates. It was noted that threshold change in behavior, as determined by algorithms, detected health disorders in more than 80% of cattle at least one d prior to identification of the same health issues by trained professionals and that changes in activity could be a useful tool for early diagnosis of health issues in dairy cows (Gonzalez et. al., 2008).

Lung Auscultation

Another such prognostic tool to monitor and provide auscultation of the lung activity is the use of an electronic stethoscope to amplify the echo and other sounds emitted from the right cranial (apical) lobe in cattle, 2 in caudal from the elbow and 2 in dorsal towards the spine (MicroBeef, 2013). The sound that is amplified from the lung is then classified into 1 of 5 categories based on a proprietary algorithm: 1) normal, 2) mild acute, 3) moderate acute, 4) severe acute, and 5) chronic (MicroBeef, 2013). A normal lung score of 1 indicates a healthy animal with no pathophysiological signs, mild acute is defined as expressing early clinical signs included reduced gains for which treatment is suggested, moderate acute is described as the presence of clinical signs and decreased performance with treatment for BRD being recommended, chronic is the demonstration of severe signs, detrimental results on performance, and permanent lung damage and extensive, immediate, and aggressive treatment is necessary (MicroBeef, 2013). Auscultation is a useful evaluation method to detect different diseases of the lung including bronchopneumonia, consolidation, pleural effusion, pulmonary emphysema, and pleuritis and provides a prognostic capability based on the amount of affected tissue.

In one study, auscultation was used to examine the thoracic cavity in 55 cattle diagnosed with lung diseases (Flock, 2004). In incurable cases, cattle were euthanized and sent to a lab for post mortem inspection. Lung auscultations prior to necropsy revealed 14.5% with mild to severe vesicular sounds, 12.7% with rough breathing patterns, 32.7% with bronchial sounds, 49.0% with rattling, splashing, or other friction sounds, 7.3% with an absence of lung sounds, and 10.9% with wheezing sounds; multiple animals were identified with a combination of sounds present. A positive diagnosis was established in 97.1% of 34 necropsied calves based on clinical and post mortem examinations (Flock, 2004). Authors observed that clinical, sonographic auscultation results generally agreed with gross pathological findings upon post mortem examination fairly well, especially in lungs with large area consolidation.

Conclusion

BRD incidence has remained relatively unchanged over the last 20 years and continues to be a tremendous loss to the cattle production industry. Current diagnostic methods lack a "gold standard" for disease diagnosis and rely heavily on the subjective appraisal of feedlot personnel. Using accelerometers to assist in BRD detection, provides an objective measure for monitoring disease. Research has made advancement in the use and understanding of behavior monitoring technology and how it relates to animal health. Accelerometers have a viable place in disease detection as animal demonstrates behavioral changes prior to being pulled by feedlot personnel for treatment. Accelerometers are an accurate, reliable, and objective health detection tool that could be beneficial for both research and commercial applications.

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CHAPTER III

BEHAVIOR VARIABLES OF FEEDLOT CATTLE CLINICALLY DIAGNOSED WITH BOVINE RESPIRATORY DISEASE VERSUS CASE CONTROL

ABSTRACT

Advancement in technology used to monitor activity in cattle could improve the ability to diagnose bovine respiratory disease (BRD) in the feedlot, as current methods are based on subjective visual assessment of clinical signs that results in low sensitivity and specificity. We hypothesized that cattle affected by BRD express detectable alterations in behavior that can be used to diagnose the disease earlier. Our primary objective was to analyze the association between changes in cattle activity in response to clinical identification of BRD in calves maintained in a commercial feedlot setting. Four arrival blocks of high risk, crossbred beef calves (109 steers, 27.1%, and 293 bulls, 72.9%; initial BW = 176.3 ± 18.8 kg) were received and housed for a 56 d evaluation period at a commercial feedlot (OT Feedyard and Research Center; Easter, TX). The cattle were processed according to standard feedlot protocol and affixed with an accelerometer device (IceQube, IceRobotics, Ltd., Midlothian, Scotland), around the metatarsus of the right rear leg, and continuous activity variables were recorded (standing time, number of

steps, number of lying bouts and motion index) relative to clinical BRD diagnosis. Activity data were summarized as daily mean ± standard error for d -6 to -1 relative to the d of clinical BRD diagnosis (d 0). Data were continuously recorded and reported in 15 min intervals and pooled by d for 56 d. Castration status, body weight, and arrival date were recorded at the time of arrival and their effects on clinical BRD morbidity and mortality rate were analyzed using the Chi-square test. Cases and controls were based on our BRD definition that utilized a combined clinical illness and depression score system. Each case calf's activity was compared with control pen mates (calves that were never BRD-diagnosed during the entire study period) at the same time relative to the disease event. Least squares means of activity variables were calculated and compared between cases and controls within d relative to BRD diagnosis of cases. Additionally, activity variables for d -5 to -3 prior to diagnosis were calculated and compared to the activity on d -1 relative to diagnosis. The percentage of calves diagnosed with BRD at least one time was 49, 23, 62, and 71.6% for block 1, 2, 3 and 4, respectively. Overall, 51.5% of the calves were diagnosed at least once with BRD, while 15.2 and 4.5% had a second and a third BRD diagnosis, respectively, during the 56-d study period. The BRD-associated mortality was 4, 2, 11, and 6.9% for block 1, 2, 3 and 4, respectively, resulting in an overall mortality of 6.0% for the total study period. A trend ($P = 0.10$) was observed for increased BRD morbidity in cattle arriving as bulls (53.9%) compared to those that were steers at the time of arrival (44.9%). Pertinent to arrival BW, a trend for a difference was noted between BW quartiles ($P = 0.06$); cattle in the lower <25% BW quartile averaged a BRD incidence of 50.7%, the intermediate 26 to 75% BW quartiles averaged 44.8%, and the upper >75% BW quartile averaged 38.7% BRD incidence. Overall, there was a

decrease in activity during the day previous to BRD diagnosis. Average ± SE standing time on the d prior to diagnosis (d -1) was 559 ± 1.94 min for cases compared to 613 ± 0.32 min in controls. The difference between d -1 and d -5 to -3 for standing time in cases was -26.6 ± 1.5 min compared to 2.33 ± 0.57 min for controls. Similarly, the number of steps on d -1 for cases and controls were 843 ± 7.8 and 1,472 ± 2.2 steps, respectively. The difference in steps between d -1 and d -5 to -3 for BRD cases was -123.1 ± 4.2 steps compared to 50 ± 2.3 steps in controls. The number of lying bouts for cases and controls was 11.4 and 14.5 on d -1, respectively. The difference between d -1 and d -5 to -3 for lying bouts in cases was -0.58 ± 0.04 min compared to 0.71 ± 0.03 min in controls. These data suggest that cattle that arrive as bulls and cattle in the lighter BW quartiles upon arrival are more prone to be diagnosed with clinical BRD compared to cattle that are steers and those with heavier BW. Furthermore, it was determined that cattle clinically diagnosed with BRD have decreased activity (as expressed by standing duration, steps taken, motion index, and lying bouts) when compared to healthy cohorts and the reduction in these variables was observed several d prior to clinical diagnosis. Accelerometer use as an objective method for diagnosing cattle may assist in the management of clinically ill cattle and provide a framework for understanding the efficacy of cattle behavior as it pertains to clinical BRD diagnoses, potentially improving the sensitivity and specificity of BRD diagnostic methods in the clinical setting.

Key Words: accelerometers, activity, bovine respiratory disease

Materials and Methods

Animals, Processing, Diet Transition

Cattle for the present study were enrolled in 4 arrival blocks consisting of approximately 100 head from the same auction market located in south Texas. Experimental procedures were approved by the West Texas A&M University Institutional Animal Care and Use Committee (# 02-10-13). In total, data from 402 crossbred beef calves (109 steers and 291 bull calves; overall initial BW = 176.3 ± 18.8 kg) was included in the present study. The cattle were transported approximately 970 km to a commercial feedlot (OT Feedyard and Research Center, LLC, Hereford, TX). Castration status was determined on the d of arrival at the feedlot. Calves were then assigned randomly to 2 different pens (n=50) that were reserved for all 4 blocks included in the study. The cattle were sorted at the time of initial processing with a 2-way sort via gate cut based primarily on castration status and secondarily on chute order. Calves from all 4 blocks were processed identically in accordance with standard operating procedures of the feedlot facility and included parenteral administration of a trivalent modified-live virus respiratory vaccine containing infectious bovine rhinotracheitis virus (IBRV) and bovine viral diarrhea virus (BVDV type 1 and 2; Titanium 3, Elanco Animal Health, Indianapolis, IN), intranasal administration of a trivalent (same antigens described previously) respiratory vaccine (Inforce 3; Zoetis, Kalamazoo, MI), and an autogenous *Mannheimia haemolytica* bacterin, administered subcutaneous (s.c.) in the neck. Additionally, a clostridium chauvoei-septicum-haemolyticum-novi-tetani-perfringens types C & D bacterin-toxoid (Covexin 8; Merck Animal Health, Madison, NJ), was administered s.c. in the neck. An anthelmintic containing ivermectin and clorsulon

(Ivomec Plus; Merial Limited, Duluth, GA) was administered s.c. in the neck, and a growth implant containing progesterone and estradiol benzoate (Component ES; Elanco Animal Health) was administered subcutaneous between the skin and cartilage in the caudal aspect of the ear. Metaphylactic treatment with tilmicosin phosphate injection (Micotil; Elanco Animal Health) was administered and a 3-d post-metaphylactic interval was implemented. Cattle were further processed with an ear-notch sample collected from the left ear to test for BVDV persistent infection, administered a unique identification tag in the right ear, horns were tipped, and calves were branded on the right hip with a hot iron. Bulls were castrated with a restrictive rubber band (Tribander, Wadsworth Manufacturing, St. Ignatius, MT, or Callicrate, No-Bull Enterprises, St. Francis, KS).

Block 1 (56 d on feed; DOF); 24 January 2014 to 21 March 2014) included 100 calves (76 bull and 24 steer calves; initial BW = 166.0 ± 17.6 kg). Accelerometers were placed on 97 head in Block 1 of which, only 96 were analyzed due to a recording failure in one of the accelerometer devices. Calves were started on a receiving ration (ration 01) consisting of 31.5% steam flaked corn (SFC), 13.5% gluten pellets, 20.0% corn silage, 20.0% cotton seed hulls, 10.0% corn condensed distiller solubles/molasses (MLDS/Mol) blend, and 5.0% liquid supplement (Table 1). They were fed ration 01 twice a d to 30 DOF (24 January 2014 to 22 February 2014) and transitioned for 7 d (23 February 2014 to 01 March 2014) on a ration that was half ration 01, fed during the first feeding, and half ration 06, fed at the second feeding. Cattle were fed for the remainder of the block (19 d; 02 March 2014 to 31 March 2014) twice a d on ration 06 consisting of 8.0% SFC, 31.0% gluten pellets, 7.0% cottonseed (CS) burrs, 48.0% corn silage, 3.0% corn stalks, and 3.0% liquid supplement (Table 2, Table 3). Cattle were fed the first time at approximately 07:36 ± 1:30 and fed the remainder of the feed call at 12:31 ± 1:00. Block 2 (56 DOF; 16 April 2014 to 11 June 2014) included 100 calves (72 bull and 28 steer calves; initial BW = 178.3 ± 16.8 kg). Accelerometers were placed on 69 head in Block 2. Cattle were started on ration 01 fed twice a d for 29 d (16 April 2014 to 14 May 2014) and transitioned for 7 d (15 May 2014 to 21 May 2014) on a ration that consisted of 50% ration 01, fed during the first feeding, and 50% ration 06, fed at the second feeding. Cattle were fed for the remainder of the block using ration 06 (21 DOF; 22 May 2014 to 11 June 2014) fed twice a d (Table 3). Average feeding times were 7:17 ± 01:22 and 12:06 ± 1:14, feeding 1 and 2, respectively. Block 3 included 100 calves (69 bull and 31 steer calves; initial BW = 175.6 ± 18.5 kg). Accelerometers were placed on 100 head in Block 3. During this block the Ice Manager software used to report activity data was updated from version 2.014 to version 2.015; however, the data output remained unchanged. Block 4 included 100 calves (74 bull and 26 steer calves; initial BW = 185.4 ± 17.4 kg). Accelerometers were placed on 98 head in Block 4. Cattle were fed ration 01 throughout the entire duration of this block (65 DOF; 17 February 2015 to 23 April 2015), however activity data were only analyzed for the first 56 DOF. Average time for the first feeding was 6:33 ± 0:21 and the average feeding time for the second feeding was 11:59 ± 1:39. Cattle were fed ration 01 throughout the entire time in this block (56 DOF; 29 October 2014 to 24 December 2014). Average time for the first feeding was 6:26 ± 0:17 and the average feeding time for the second feeding was 10:29 ± 4:19.

Bovine Respiratory Disease Case Definition

The clinical bovine respiratory disease (BRD) diagnosis of calves was determined by visual appraisal of clinical signs (nasal/ocular discharge, labored breathing, unresponsive to human approach, lowered head, depressed stance, slow movements, stands at the back of the group, weakness, and incoordination) consistent with the disease according to trained feedlot personnel. A clinical illness score (CIS; Table 4) was determined as follows: 0) indicated a normal healthy calf, 1) denoted a slightly ill calf as it expressed clinical signs of gauntness and nasal and/or ocular discharge, 2) implied that a calf was moderately ill and demonstrated clinical signs of gauntness, nasal and/or ocular discharge, coughing or laboring breathing and tended to lag behind pen mates, 3) designated a severely ill animal with clinical signs of purulent nasal and/or ocular discharge, labored breathing and was nonresponsive, and 4) moribund cattle were near death and non-responsive. A depression score (Table 5) was also determined daily: 0) normal and expressed no signs of depression; 1) slightly depressed animals were observed to be slightly slower then pen mates but is still alert and doesn't show signs of weakness; 2) moderately depressed cattle maintain a depressed stance with head hung, but will raise head upon approach, animals will also fall towards the back of the group and may express signs of weakness and lack of coordination; 3) severely depressed animals are very weak, falls towards the back of the group, and only raises its head when approached closely; 4) moribund cattle are very near death and non-responsive. Feedlot personnel were trained to recognize the signs described for both CIS and depression scores, and cattle were pulled according to these methods. The CIS was used to describe the severity of the illness of cattle, describing the degree of gauntness, nasal and ocular discharge, and labored breathing patterns. Similarly, the depression score was used to describe the severity of depression demonstrated by cattle describing changes in motility and alertness.

Calves were considered a clinical BRD case for the current study if: a) a score of 1 was determined for both the CIS and the depression score method, or b) a score of ≥ 2 was determined for either scoring method. Morbidity and mortality records were acquired from the in house data management system, Animal Health International, Inc. (Greeley, CO). Calves not determined to display signs of BRD during the study (control), calves having a BRD diagnosis and treated only once (BRD1), calves having a BRD diagnosis twice (BRD2), and calves that were diagnosed for BRD and treated 3 times (data not shown). Calves with the disease status of BRD1 were included in BRD2.

Cattle were treated in accordance to a pre-defined antimicrobial regimen upon recommendation of the consulting veterinarian of the facility. After expiration of the post treatment interval (PTI) cattle were eligible for additional antimicrobial treatment (BRD2 and BRD3, respectively) if clinical signs were presented according to the previously described BRD case definition. Antimicrobial treatments were administered to clinically ill cattle following the pre-defined antimicrobial treatment regimen consisting of: treatment for BRD1 included ceftiofur crystalline free acid (Excede, 5-d PTI, Zoetis, Kalamazoo, MI), 1.5mL/45.5 kg, s.c. at the base of the caudal aspect of the ear. After being diagnosed with BRD2, treatment comprised of florfenicol (Nuflor, 3-d PTI; Merck Animal Health, Madison, NJ), 3mL/45.5 kg, s.c. in the neck. A third BRD diagnosis (BRD3) included treatment with oxytetracycline hydrochloride injection (Oxytet 100; Norbrook Inc., Lenexa, KS), 5mL/45.5 kg, s.c. in the neck. All cattle treated for BRD were returned to their home pen immediately following antimicrobial treatment; there was no separation of healthy calves from calves diagnosed with BRD.

Accelerometers

Cattle were affixed with an accelerometer device (IceQube, IceRobotics, Ltd., Midlothian, Scotland), around the metatarsus of the rear right leg. Activity data from 364 head were continuously logged in this study. The accelerometer devices are a 3-axis accelerometer that generates a change in electrical output voltage relative to the position of the device. The output voltage is translated via proprietary algorithm into duration of standing and lying time (min), number of steps taken, number of lying bouts, and a proprietary motion index calculation allowing a detailed report on activity to be quantified. Data from the accelerometers was generated in 15 min intervals that was then pooled to establish means for each activity variable by d. Alternatively, non-pooled data were analyzed as continuous behavior data over a 24 h period for cases and controls.

Standing/lying: determined as a sensor passes a specific threshold on a vertical/horizontal plane.

Lying bouts: the frequency that each lying activity occurred.

Motion index: a proprietary index calculated by acceleration on all 3 axes indicative of overall activity.

Step count: the number of upward movements captured by the device in regards to the force utilized.

Data were analyzed to determine the mean ± standard error for the time period of d -6 to -1 relative to clinical BRD diagnosis. As data were likely confounded due to pen removal to administer the antimicrobial treatment regimen, activity on the d of treatment (d 0) was omitted from the current analysis.

Statistical Analysis

Data were organized in spreadsheets (Microsoft Corp., Seattle, WA) and analyzed with statistical software (SAS Inst. Inc., Cary, NC; version 9.2) with individual animal serving as the experimental unit. Activity variables (reported in 15 min intervals) were averaged by d and organized to compare controls to clinical BRD cases. Each case animal's activity was compared to its control pen mates during the same time relative to BRD treatment of the case. Control animals for this study were defined as calves never affected or treated for BRD clinical signs throughout the duration of the 56-d study. Averages for activity variables (step count, motion index, lying bouts and standing time) were calculated for cases 6 d prior to clinical BRD diagnosis and compared to the averages for control calves for the same period of time. Day -1 was defined as the d before animals were identified as a clinical BRD case by animal health technicians; likewise, d -6 was six d before an animal was diagnosed with clinical BRD.

Additionally, the total step count for cases and controls was analyzed using downloaded accelerometer data in 15 min intervals to provide activity variables reported on a 24 h basis, to elucidate differences in behavior between cases and controls throughout the d. Least squares means within a day relative to BRD diagnosis of cases were calculated and compared between cases and controls using PROC GLM. Frequencies were calculated for demographic information and categorical outcomes (treatment and death). Statistical analysis to determine significant associations in the secondary objective between outcomes of interest and suggested explanatory variables were analyzed by Chi-square test and logistic regression analysis (PROC FREQ and PROC GLIMMIX, respectively). Explanatory variables included block, arrival BW quartile (low (Q1; lower 25% of BW within Block); intermediate (Q2-Q3; intermediate 25 to 50% BW within Block); and high (>Q3; upper 25% of BW within Block), and castration status (bull or steer) upon arrival. Least squares means were calculated for each of the activity variables of cases and controls and differences within d relative to BRD diagnosis were determined using PROC GLM. For each of the statistical analyses, significance was established for a *P*-value ≤ 0.05; whereas, a trend was considered for a *P*-value between 0.06 and 0.10.

Results and Discussion

Demographics

Among the current study population, the percentage of calves diagnosed with BRD at least one time was 49, 23, 62, and 71.6% for blocks 1, 2, 3, and 4, respectively. Overall, 51.5% of the calves were diagnosed at least once with BRD, while 15.2 and a 4.5% had a second and third BRD diagnosis during the study period. Other studies have shown that recently weaned single source calves maintained a morbidity rate of 22.2% and recently weaned, commingled calves demonstrated a morbidity rate of 31.9% (Smith, 2010). Furthermore, it has been observed that cattle having received metaphylactic treatment with tilmicosin resulted in decreased BRD morbidity in an economically feasible manner when compared to cattle that were never treated (Tennant et. al., 2014); tilmicosin resulted in a 3.8 kg increase in final BW, and a 4.8% increase in ADG.

Comparatively, the overall incidence of BRD across the industry is gradually increasing and is currently upwards of 16.2% (USDA, 2013). Mortality per block was 4, 2, 11, and 6.9% for blocks 1, 2, 3, and 4, respectively, resulting in an overall mortality rate of 6.0% for the total study period.

Arrival BW and castration status

A tendency (P = 0.10) for increased BRD morbidity in the intact bulls upon arrival (53.9%) was observed compared to those that were steers at the time of arrival (44.9%). Other studies found similar tendencies with steers, stratified by body weight, experiencing the additional stress of castration upon arrival being 92% more likely to suffer from morbidity and 3.5% more likely to die compared to previously castrated steers; however, this data could possibly be confounded due to preconditioning or other management practices prior to arrival (Snowder et. al., 2006; Duff et. al., 2007). In a retrospective analysis, the odds ratio for bulls being diagnosed with BRD once was 3.32 times greater and diagnosed twice was 4.02 times greater than that of steers (Richeson et. al., 2013). Castration increases morbidity and results in increased stress and inflammation. Thus, the added stress of castration upon arrival potentially has a more significant impact on BRD incidence than cattle that arrive as steers (Richeson et. al., 2013, Duff et. al., 2007, Snowder et. al., 2006). The effect of gender on BRD outcome is further influenced by arrival weight and season of arrival (Babcock et al., 2013; Cernicchiaro et. al., 2013) as well as other management factors imposed in steers, but not bulls that may reduce the risk of BRD.

A trend for a difference (*P* = 0.06) in BRD morbidity was observed between each of the BW quartiles; cattle in the lightest <25% BW quartile had an average BRD incidence rate of 50.7%, the intermediate BW category (26 to 75% BW quartile) averaged 44.8%, and the heaviest >75% BW quartile averaged 38.7% BRD morbidity rate (Table 6). Similarly, it was reported in previous studies that increased arrival weight results in decreased morbidity risk (Babcock et al., 2013; Cernicchiaro et. al., 2013; Taylor et. al., 2010). Calves weighing less than average were 1.4 times more likely to be diagnosed with BRD (Gummow, 2000). The benefit of additional weight at the time of arrival may be a consequence of preconditioning programs implemented before arrival (Taylor et. al., 2010). However, a clear association between decreased morbidity rates with increased arrival weight has yet to be established (Taylor et. al., 2010).

Activity change in cases versus controls relative to BRD diagnosis

Activity or behavior is one of the first aspects of an animal affected by disease and is the most common parameter used in the clinical diagnosis of disease, including BRD (Szyszka et. al., 2012). It has been concluded that IceTags, an accelerometer manufactured by the same company and similar to the IceQube devices used in this study, provide valid standing/lying duration, number of steps, and frequency of activity with no effect noted for placement of the accelerometer. Furthermore, studies have concluded that IceTags could be “reliably used in research…to measure activity” (Gibbons et. al., 2012; Nielsen, et. al., 2010; Trénel, et. al., 2009). Authors reported that automated measures of acceleration (Hobo Pendant G Acceleration Data Logger, Onset Computer Corporation, Pocasset, MA) are practical to determine step count and gait (de Passillé, et. al., 2010). Superb agreement between accelerometers (GP1 SENSR;

Reference LLC, Elkader, IA) and video recording between lying and standing activity has been observed with 99.2 and 98% accuracy, respectively, and good agreement on walking (step count) with a reported 67.8% accuracy. Investigators concluded, "accelerometers provided an accurate, remote measure of cattle behavior" (Robert et. al., 2009). Change in activity may indicate early BRD morbidity, as number of steps decrease after infection, but this change fails to correlate with severity of disease (Szyszka et. al., 2012, Hanzlicek, 2010).

Average ± SD standing duration on the d prior to diagnosis (d -1) was 559 ± 1.94 min for cases compared to 613 ± 0.32 min in controls. The difference between d -1 and d -3 to -5 for average standing time in cases was -26.6 ± 1.5 min compared to 2.33 ± 0.57 min in controls. Similarly, number of steps on d -1 for cases and controls were 843 ± 7.8 and 1,472 ± 2.2 steps, respectively. The difference between d -1 and d-3 to d-5 for number of steps in cases was -123.1 ± 4.2 steps compared to 50 ± 2.3 steps in controls. The duration of lying bouts for cases and controls was 11.4 and 14.5, respectively. The difference between d -1 and d -3 to -5 for lying bouts in cases was -0.58 ±0.04 min compared to 0.71 ± 0.03 min in controls.

The BRD cases showed a decrease ($P < 0.0001$) in step count (the number of upward movements captured by the device in regards to the force utilized) on each d from d -6 to -1 when compared to the step count of controls. Cases had a decreased step count on d -6; 1,185 steps were observed for cases compared to 1,453 steps in control, and decreased to 1,111 steps on d -5 and continued to decrease to 986 steps on d -4. On d -3, step count for cases had stabilized at approximately 860 and remained constant until d -1 (851 steps for d -3, 888 steps for d -2 and 840 steps for d -1). Comparatively, the step count of controls remained relatively static averaging 1,460 steps per d (Figure 1). Likewise, the motion index results revealed a similar difference between cases and controls ($P < 0.0001$ for d -4 to -1 and $P = 0.008$ for d -5). Cases demonstrated a consistent decrease in motion index from d -5 to -1 compared to a greater, but static motion index observed for controls during this same time. However, d -6 motion index was not different ($P > 0.05$) to that of controls (Figure 2). This suggests that the motion index, and therefore the overall activity in clinically ill cattle is altered 5 d prior to clinical BRD diagnosis. Cases had an average motion index of 98.6 on d -6, yet the motion index decreased in cases such that a difference on d -5 existed ($P = 0.008$; 85.13 vs. 97.8) and d -4 ($P < 0.0001$; 79.2 vs. 97.9). Lying bouts in cases were decreased ($P < 0.0001$) from d -6 to -1 compared to controls. Cases ranged from 12.2 lying bouts (d -6) to 11.3 (d -3) but remained relatively consistent from d -6 to -1. Likewise, controls remained constant in the number of lying bouts ranging from 14.6 (d -5) to 14.8 (d -3; Figure 3). Differences in standing time ($P < 0.05$) was observed between cases and controls; however, a bimodal pattern was observed in cases with the greatest duration of standing time on d -5 (608 min/d) and the least amount of standing time was observed on d -1 (559 min/d). Comparatively, controls remained relatively constant in their duration of standing time across d -6 to -1, with approximately 611 min/d. Differences in standing time were observed on d -3 ($P = 0.003$; 562 min in cases compared to 611 min in controls) and on d -1 ($P = 0.001$; 559 min in cases compared to 613 min in controls; Figure 4).

Temporal activity in cases versus controls

When steps were averaged and displayed for cases and controls over a 24-h time period, bimodal step count patterns were observed for both cases and controls; however, controls expressed more noticeable peaks and valleys. The first increase in steps was noted at approximately 05:00 in both cases and controls; this was likely in concert with the time of initial feeding, 06:56 ± 01:07. Activity decreased at approximately 12:00, around the time of the second feeding, which was 11:31 ± 03:02. The second peak in steps occurred in both cases and controls beginning around 16:30 and this decreased at approximately 21:00 for controls and 19:30 for cases. A decrease in number of steps taken by clinical cases was observed throughout the entire d with a greater decrease in number of steps observed later in the d as cases step count became more variable (Figure 5). An inverse bimodal pattern was observed in the difference in the step count (cases - controls). A slightly less step count was noted for the first peak, approximately 06:00 to 11:45, and a greater decrease in total steps was observed for the second peak, approximately 15:45 to 22:30. A decreased number of steps were also observed after the second daily feeding event, which occurred between approximately 13:00 to 15:00 (Figure 6).

Prior to infection, cattle spend a greater amount of time standing than lying down, and this activity is inverse 10 h after an animal has been infected, associated with clinical depression (Szyszka et. al., 2012). It was noted that the most significant behavior changes after being exposed to a health challenge, was that the duration of lying time increased and the frequency of lying bouts decreased when compared to healthy cattle (Szyszka et. al., 2012). Consequently, continuous monitoring of activity with accelerometers is a promising tool for novel disease detection, as infection affects activity and can assist in identifying sick animals earlier especially when coupled with other diagnostic methods (Wolfger et. al., 2015; Moya et. al., 2015; Szyszka et. al., 2012). Activity has also been used to detect behavior changes due to lameness (Alsaaod, et. al., 2012; Mazrier, et. al., 2006), castration (White, et. al., 2008), and estrus detection (Saint-Dizier et. al., 2012; Løvendahl et. al., 2008; Roelofs et. al., 2005; Koelsch et. al., 1993).

Conclusions

These data suggest that cattle that arrive as bulls and cattle comprised of lighter BW upon arrival are more likely to be diagnosed with clinical BRD opposed to cattle that are steers and those with a heavier initial BW. Similarly, cattle with intermediate BW were diagnosed more frequently with BRD then those in heavy BW quartile upon arrival. Furthermore, it was observed that cattle clinically diagnosed with BRD have decreased activity during the days previous to BRD diagnosis (as indicated by a decrease in standing duration, steps taken, motion index, and lying bouts) when compared to healthy cohorts. Incorporating this knowledge into an objective method for diagnosing cattle may assist in the identification and management of cattle affected with BRD, thus providing a framework for understanding cattle behavior in the commercial feedlot setting as it pertains to clinical BRD diagnoses, thus improving diagnostic methods.

Current BRD diagnostic methods are based largely on subjective visual appraisal and have remained unchanged over the last several decades. A critical factor in BRD control is timely diagnosis and identification of clinical signs. A measurable, reliable, and repeatable means of field diagnosis that can accurately identify BRD in a cost effective manner is warranted. With new technology such as accelerometers, capable of continuous monitoring, advancements can be made in the understanding of activity relative to cattle health status and performance. Accelerometers and other technological tools may possess commercial application and potentially decrease time needed to accurately diagnose BRD morbidity in the commercial production setting. Improved control of this disease can only be accomplished with increased understanding of the interactions between the host immune and respiratory systems, infective pathogens, and the environment. Before technology capable of behavior quantification can be successfully incorporated into the commercial feeding industry, it must be cost-effective and practical for use in the industry. Thus, there must be an improvement in technology coupled with a significant decrease in price before this technology becomes a realistic option to use in the commercial feedlot industry.

Table 1. Calculated ingredient composition for ration 1.

Ingredient	Percentage[1]
Steam flaked corn (SFC)	31.5
Corn Gluten pellets	13.5
Corn silage	20.0
Cottonseed hulls	20.0
Corn condensed distiller solubles/molasses Blend	10.0
Liquid Supplement	5.0

[1]Values are reported on a dry matter (DM) basis.

Table 2. Calculated ingredient composition for ration 6.

Ingredient	Percentage[1]
Steam Flaked Corn	8.0
Corn Gluten pellets	31.0
Cottonseed burrs	7.0
Corn Silage	48.0
Corn Stalks	3.0
Liquid supplement	3.0

[1]Values are reported on a dry matter (DM) basis.

Table 3. Diet transition during the 56 day feeding period.

Ration Type	Ration (R)	Days Fed	Percentage	
Starting Ration	01	29-30	100	Fed twice daily
Transition Ration	01/06	7	50/50	R01 fed at the first feeding R06 fed at the second feeding
Finishing Ration	06	36-37+	100	Fed twice daily

Ration 01: 31.5% steam flaked corn (SFC), 13.5% gluten pellets, 20.0% corn silage, 20.0% cotton seed hulls, 10.0% corn condensed distiller solubles/molasses (MLDS/Mol) blend, and 5.0% liquid supplement (Table 1) Ration 06: 8.0% SFC, 31.0% gluten pellets, 7.0% cottonseed (CS) burrs, 48.0% corn silage, 3.0% corn stalks, and 3.0% liquid supplement (Table 2). Cattle were fed the first time at approximately 07:36 ± 1:30 and fed the remainder of the feed call at 12:31 ± 1:00.

Table 4. Definition of clinical illness score.

Clinical Illness Score	Description	Appearance
0	Normal	Normal
1	Slightly ill	Gaunt, nasal/ocular discharge
2	Moderately ill	Gaunt, nasal/ocular discharge, lags behind other animals in the group, cough, labored breathing
3	Severely ill	Purulent nasal/ocular discharge, labored breathing, not responsive to human approach
4	Moribund	Near death

Clinical illness score (CIS) was determined by visual appraisal daily by trained animal health care professionals and used with a depression score to determine clinical illness of feedlot cattle. Calves were considered a clinical BRD case if: a) a score of 1 was scored on both the CIS method and the depression score method (Table 4), or b) a score of ≥ 2 was achieved for either scoring method.

Table 5. Definition of depression score.

Depression Score	Description	Appearance
0	Normal	Normal, no signs of depression
1	Slightly Depressed	Slower than pen mates but still perks up when approached and does not appear weak, actively follows your movements with a raised head
2	Moderately Depressed	Stands with head lowered, will perk up when approached but will return to depressed stance, moves slowly and falls towards back of group, may display signs of weakness such as incoordination
3	Severely Depressed	Obviously very weak, difficulty in moving with group, raises head only when approached closely
4	Moribund	Near death, non-responsive to human approach

Depression score was determined visual appraisal daily by trained animal health care professionals and used with a CIS to determine clinical illness of feedlot cattle. Calves were considered a clinical BRD case if: a) a score of 1 was scored on both the CIS method (Table 3) and the depression score method, or b) a score of ≥ 2 was achieved for either scoring method.

Table 6. Percentage of steers diagnosed with clinical BRD in a commercial feedlot for 56 days on feed according to body weight (BW) quartile.

Lower BW Quartile (<25%)	**Intermediate BW Quartile (26 – 74%)**	**Upper BW Quartile (>75%)**
50.7[a]	44.8[b]	38.7[c]

Body weight quartile was determined with weight upon arrival. The BRD morbidity rate for cattle categorized in light (<25%), intermediate (26 to 74%), and heavy (>75%) initial body weight quartiles was different as indicated by unlike letters (*P* = 0.06).

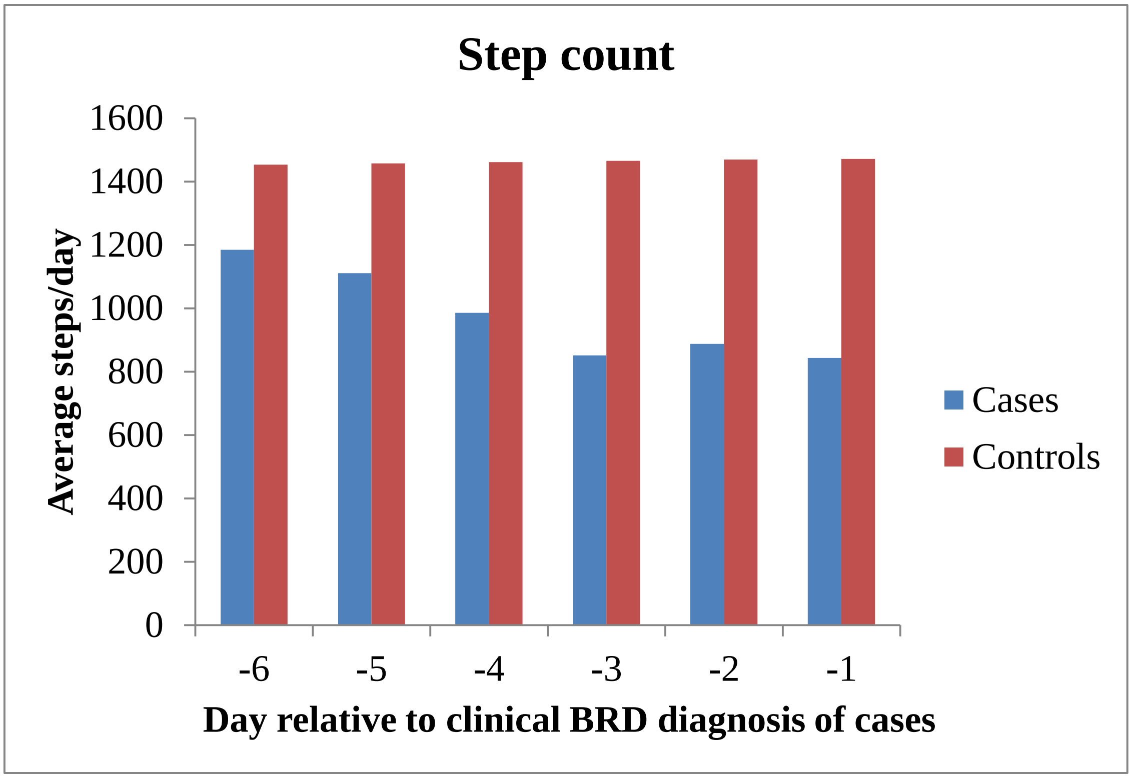

Figure 1. Average step count of cases and controls relative to clinical BRD diagnosis of cases for steers fed in a commercial feedlot for 56 days on feed. Calves were considered a clinical BRD case if: a) a score of 1 was scored on both the CIS method (Table 3) and the depression score method (Table 4), or b) a score of ≥ 2 was achieved for either scoring method. Calves not determined to display signs of BRD during the study were determined to be the control. D -1 is defined as the d before animals were identified as a clinical BRD case by animal health technicians; likewise, d -6 was six d before an animal was diagnosed with clinical BRD. On d 0, behavior data was omitted from the analysis due to the imposed change in behavior as an animal is moved from their home pen to a hospital facility for treatment and then returned to the home pen. All means between cases and controls within d differ; $P < 0.0001$.

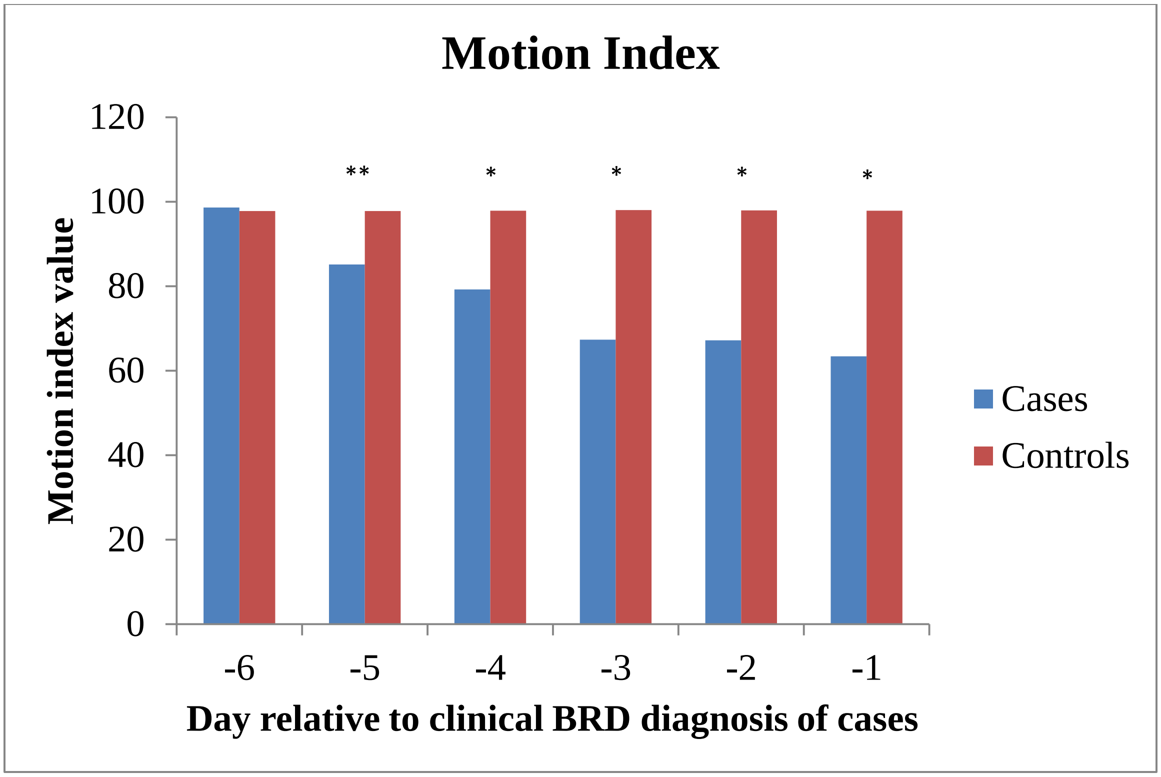

Figure 2. Average motion index value for cases and controls relative to clinical BRD diagnosis of cases for steers fed in a commercial feedlot for 56 days on feed. Calves were considered a clinical BRD case if: a) a score of 1 was scored on both the CIS method (Table 3) and the depression score method (Table 4), or b) a score of ≥ 2 was achieved for either scoring method. Calves not determined to display signs of BRD during the study were determined to be the control. D -1 is defined as the d before animals were identified as a clinical BRD case by animal health technicians; likewise, d -6 was six d before an animal was diagnosed with clinical BRD. On d 0, behavior data was omitted from the analysis due to the imposed change in behavior as an animal is moved from their home pen to a hospital facility for treatment and then returned to the home pen. Differences in means are denoted as *P < 0.0001; **P = 0.008.

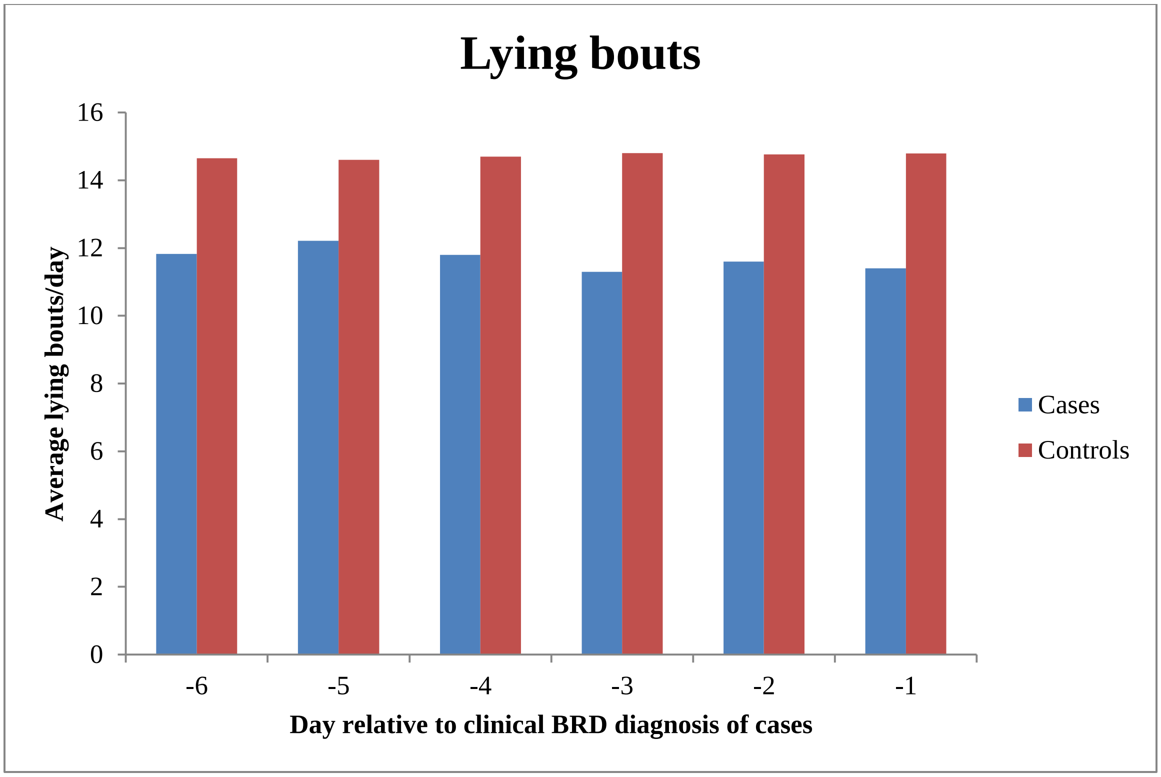

Figure 3. Average lying bouts for cases and controls relative to clinical BRD diagnosis of cases of steers fed in a commercial feedlot for 56 days on feed. Calves were considered a clinical BRD case if: a) a score of 1 was scored on both the CIS method (Table 3) and the depression score method (Table 4), or b) a score of ≥ 2 was achieved for either scoring method. Calves not determined to display signs of BRD during the study were determined to be the control. D -1 is defined as the d before animals were identified as a clinical BRD case by animal health technicians; likewise, d -6 was six d before an animal was diagnosed with clinical BRD. On d 0, behavior data was omitted from the analysis due to the imposed change in behavior as an animal is moved from their home pen to a hospital facility for treatment and then returned to the home pen. All means between cases and controls within d differ; P<0.0001.

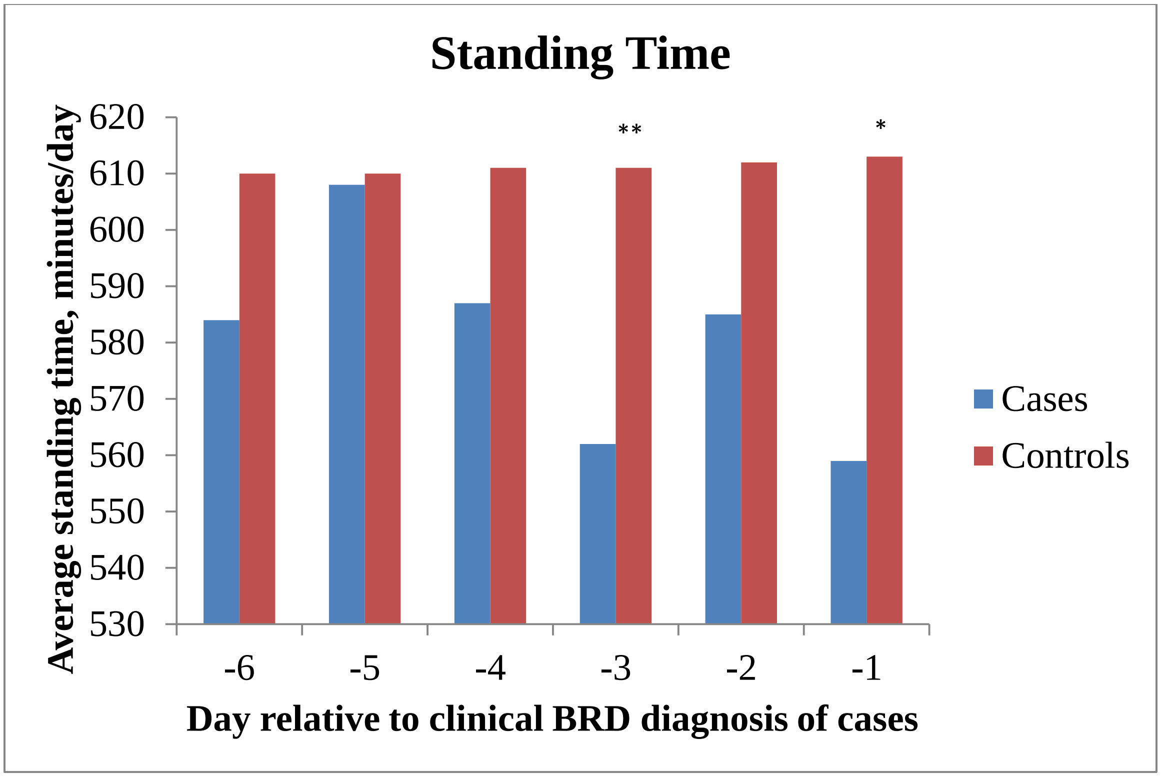

Figure 4. Average standing time for cases and controls relative to clinical BRD diagnosis of cases of steers fed in a commercial feedlot for 56 days on feed. Calves were considered a clinical BRD case if: a) a score of 1 was scored on both the CIS method (Table 3) and the depression score method (Table 4), or b) a score of ≥ 2 was achieved for either scoring method. Calves not determined to display signs of BRD during the study were determined to be the control. Day -1 is defined as the d before animals were identified as a clinical BRD case by animal health technicians; likewise, d -6 was six d before an animal was diagnosed with clinical BRD. On d 0, behavior data was omitted from the analysis due to the imposed change in behavior as an animal is moved from their home pen to a hospital facility for treatment and then returned to the home pen. Differences in means are denoted as *P = 0.001;**P = 0.003.

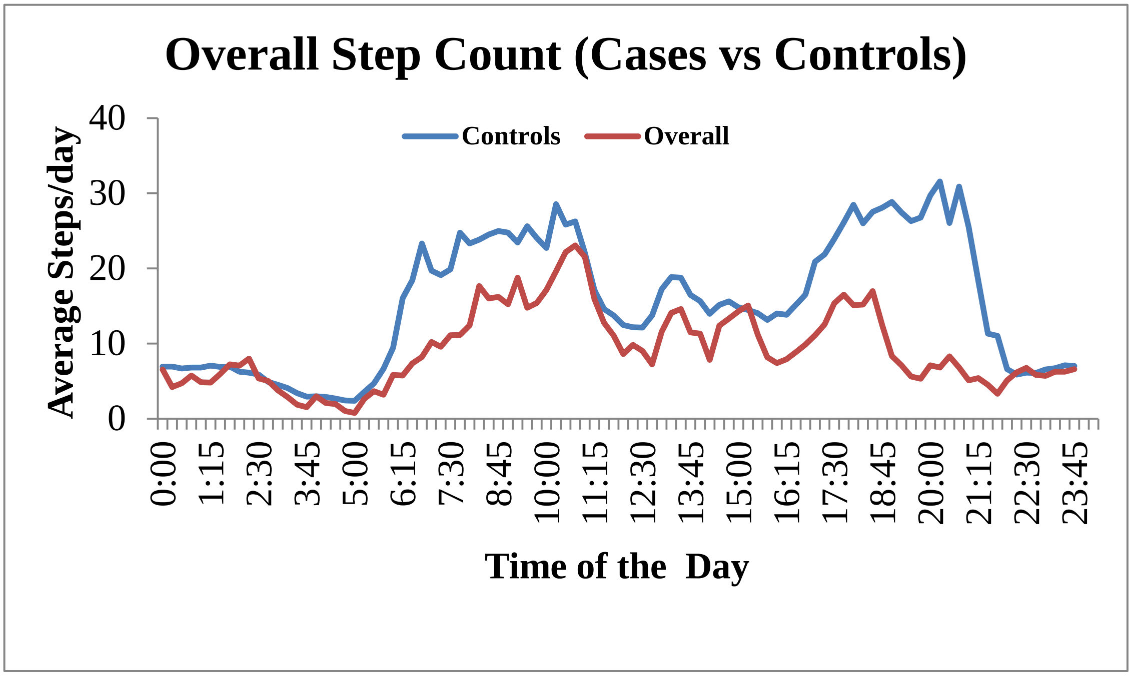

Figure 5: Average number of steps for cases and controls expressed over 24 hour time in a commercial feedlot for 56 days on feed. Calves were considered a clinical BRD case if: a) a score of 1 was scored on both the CIS method (Table 3) and the depression score method (Table 4), or b) a score of ≥ 2 was achieved for either scoring method. Calves not determined to display signs of BRD during the study were considered a control. Average time of initial feed delivery = 06:56 ± 1:07 and is denoted by the first vertical bar within the figure. Average time of second feed delivery = 11:31 ± 3:02 and is denoted by the second vertical bar within the figure.

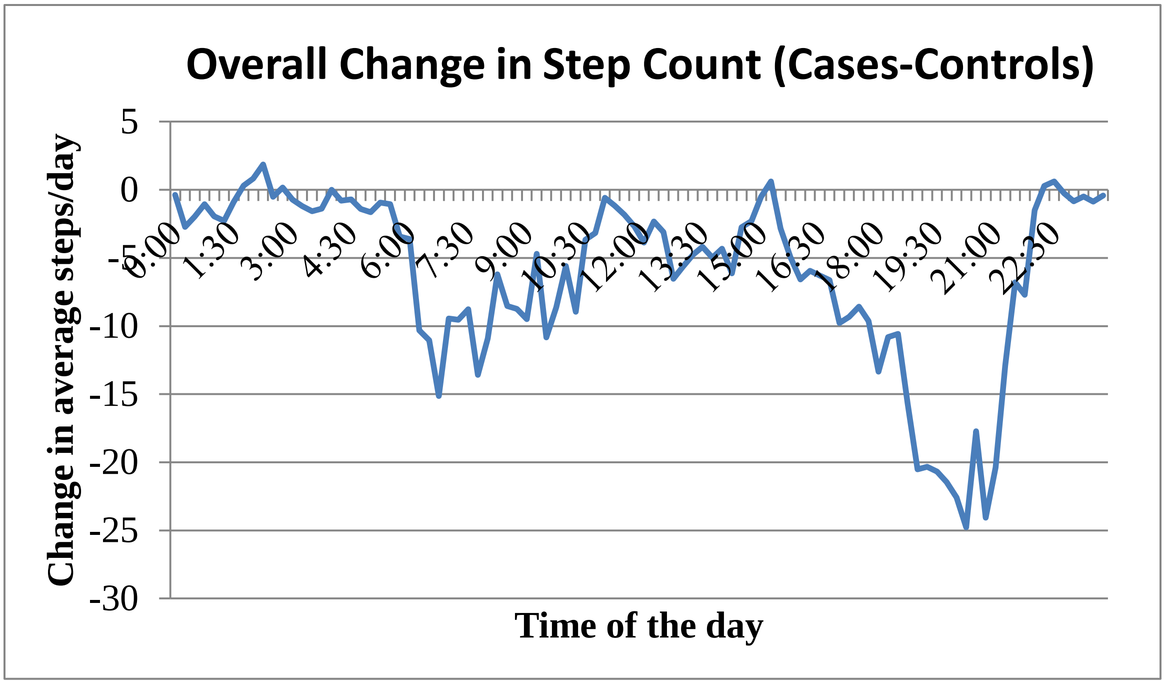

Figure 6. Average change in step count of cases relative to control over a 24 hour time in a commercial feedlot for 56 days on feed. Calves were considered a clinical BRD case if: a) a score of 1 was scored on both the CIS method (Table 3) and the depression score method (Table 4), or b) a score of ≥ 2 was achieved for either scoring method. Calves not determined to display signs of BRD during the study were consider a control.

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