EVALUATION OF PERFORMANCE IN YEARLING CROSSBRED STEERS FOLLOWING BOVINE VIRAL DIARRHEA VIRUS CHALLENGE

A Dissertation

By

CHASE ANTHONY RUNYAN

Submitted to the Office of Graduate and Professional Studies of
Texas A&M University
in partial fulfillment of the requirements for the degree of

DOCTOR OF PHILOSOPHY

December 2013

Major Subject: Animal Science

ABSTRACT

This study investigated the effects of vaccine type, sire, day, threshold rectal temperature status, and their potential interactions on growth, daily feed intake and daily feed bunk frequency in response to a standardized Bovine Viral Diarrhea Virus (BVDV) challenge. Yearling, F_2 and F_3 Nellore-Angus steers (n = 380) from the Texas A&M McGregor Genomics herd were utilized over 4 years, and were stratified by sire over three vaccine groups of modified-live (MLV), killed (KV), and non-vaccinated (NON). Vaccines were used in accordance to label directions, and MLV steers were separated from KV and NON steers for 7 to 10 days to prevent transmission of viral particles. All steers were intranasally challenged with BVDV type 1b strain CA0401186A on day 0 of each year. Clinical signs of illness and feeding behavior data were collected daily, while rectal temperature and weight records were collected at days 0, 3, 7, 10, 14, 28, and 42 post-vaccination.

The influence of sire was a significant source of variation as both a main effect or as an interaction term for all response variables analyzed. Vaccine type was a significant source of variation as components of interaction terms; lower ($P < 0.05$) mean rectal temperature was seen in MLV as compared to KV and NON steers. Variation from sire and vaccine type interaction suggests the potential of matching genetic profiles and vaccine protocols to achieve optimum levels of production measures.

Daily feed intake and daily bunk visit frequency tended to decrease through day 7, but these traits should be interpreted separately due to the effects of sire and sire by vaccine type interactions. Higher number of bunk visits did not explain levels of intake within some sire groups and vaccine groups. Lung tissue disruption based on color scores of 3 or 4, on 5-point scale was present in more than 65% of cattle that did not have elevated rectal temperature above 40^{o}C, the threshold basis for provision of antibiotic treatment. Interactions involving sire, vaccine type or rectal temperature status with other factors in this trial illustrates complexity regarding interpretation of cattle health impacts on production traits.

ACKNOWLEDGEMENTS

The first person I would like to acknowledge is Dr. Andy Herring and this acknowledgment is not near enough. Thank-you for allowing me this opportunity Dr. Herring, I am extremely grateful for your guidance. Dr. Jason Sawyer, Dr. Tom Welsh, and Dr. Penny Riggs are next, as I have a great deal of appreciation for their service to my Ph.D. committee. I would like to give thanks to Travis Roitsch, Kerry Dean, and the Beef Cattle Systems Research Unit crew for their efforts and for always picking up the phone. I would also like to express thanks to the long list of fellow graduate students who've been a part of this project, many of you have become life-long friends and for that I'm even more thankful. I would like to acknowledge Dr. Julia Ridpath at the USDA-ARS National Animal Disease Center in Ames, IA for supplying the virus inoculum and the Texas A&M AgriLife Research Texas Beef Competitiveness program for project funding. Finally, I especially would like to recognize my parents Mark and Lisa Runyan, brothers Jason Runyan and Tell Runyan, and my wonderful wife Morgan Runyan for all of their unconditional love, encouragement, and support.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

Page

INTRODUCTION

Bovine Respiratory Disease (BRD) remains one of the most common and expensive health related threats to the U.S. beef cattle industry. Added costs accrue from the effects of reduced animal performance, prevention methods, antibiotic therapy, and in severe cases animal death. In spite of prevention and treatment efforts, there is evidence that morbidity manifests as sub-clinical illness and can result in irritations of the lungs or pulmonary tissue damage in animals that have never been identified for illness. Breed differences pertaining to BRD occurrences have been reported but the understanding of the genetic influences of BRD is limited. Treatment and prevention methods against BRD have been largely disputed as well. Vaccine efficacy and vaccine strategy also remains largely questioned as does antibiotic use in current treatment regimes. One of the key viral agents of the BRD complex, Bovine Viral Diarrhea Virus (BVDV), threatens cattle production systems not only from its threat of morbidity and mortality from transient infection, but also the immune suppressive capabilities and the incidence of cattle persistently infected with the virus.

The objectives of this dissertation are to investigate the relationships of vaccination strategy and health related measures with production traits of feed intake and growth performance of cattle with known genetic background following a Bovine Viral Diarrhea Virus challenge.

LITERATURE REVIEW

Animal health can be summarized as the overall physical condition and well-being of animals. In beef cattle, morbidity (sickness) can result in economic losses due to reduction in performance and create additional costs associated with treatment or mortality (death loss). Smith (1998) concluded that morbidity and mortality in growing cattle on pasture and in feedlots can be the result of numerous disorders, but most commonly respiratory and digestive associated diseases.

Bovine Respiratory Disease

Bovine Respiratory Disease (BRD) is a broad, multifaceted disease which includes viral and bacterial agents. Occurrences of BRD are the result of pathogenic bacteria and the presence of one or more viral infections (Daniels et al., 2000). The viral agents that contribute to BRD are Bovine Herpes Virus-1 (BHV-1), Parainfluenza-3 virus (PI-3), Bovine Respiratory Syncytial Virus (BRSV) and Bovine Viral Diarrhea Virus (BVDV). Suppression of immune response activity by these viruses can facilitate development of bacterial pneumonia caused by *Mannheimia haemolytica*, *Pasteurella multocida*, *Histophilus somni*, and *Mycoplasma* spp. (Fulton et al., 2000a; 2002; 2006). In addition to viral and bacterial exposure, reduced disease resistance typically occurs under instances of stress. Stress in growing cattle systems includes transportation, co-mingling of different groups of animals, weaning, and processing creates scenarios where cattle immune systems are compromised, thus providing a scenario for higher BRD incidence (Blecha et al., 1984). Duff and Galyean (2007) also discussed that BRD

has the most prevalent occurrence following shipping, especially from auction barns where cattle are co-mingled. Furthermore, (Edwards 2010) stated that cattle are at a higher risk early in the feeding period when viral and bacterial exposure is compounded with high stress during arrival periods. Pre-exposed cattle of various geographic locations, breed types, immune status, and management systems are comingled in the feed yard or shortly before arrival through regional auctions.

Bovine Respiratory Disease costs

In terms of financial strain on the U.S. cattle industry, BRD incidence is a burden in beef cattle operations of an enormous scale. Griffin et al. (1997) summarized an estimated annual loss of $750 million due to BRD incidence. Chirase et al. (2001) reported a similar range of estimated loss of $800 to $900 million annually from death loss occurrence, reduced feed intake and reduced weight gain, and treatment-associated costs. McNeill et al. (1996) summarized Texas A&M Ranch to Rail data and concluded that a difference of $93 added expense per animal was attributed to cattle treated for BRD versus cattle that were not treated. In terms of additional costs related to treatment alone, NAHMS (2000) reported that the average cost of treatment for one animal in a large feedlot setting (8,000 head or more capacity) was $16.26, and the cost of treatment for one animal in a small feedlot setting (1,000 to 7,999 head capacity) was $11.09; NAHMS (2013a) showed those figures have increased over the past decade. Table 1 displays the cost comparisons of single BRD cases from 1999 NAHMS as compared to 2011 NAHMS reports for small and large feedlot settings.

Table 1. Cost comparisons of single BRD case 1999 NAHMS vs. 2011 NAHMS

	1,000 – 7,999 capacity	8,000 or more capacity
1999 NAHMS	$11.09	$16.26
2011 NAHMS	$23.40	$23.90

Coupling the incidence of morbidity due to BRD and the negative economic impact is an industry wide concern. Galyean et al. (1999) calculated that 52% of U.S. feedlot morbidity was a result of BRD. Snowder et al. (2006) reported incidence of BRD as high as 43.8% in 18,112 cattle over a 15-yr period from herds at the US Meat Animal Research Center at Clay Center, NE. Edwards et al. (1996) reported morbidity of up to 82% as the result of BRD and summarized that morbidity and mortality from BRD was most common in the first 45 days after arrival at the feedlot.

Bovine Respiratory Disease clinical diagnosis

Traditionally, illness in cattle has been identified by changes in behavior that differ from what is expected in "healthy" cattle. Trained animal handling personnel identify illness based on signs of depression, increased rectal temperature, lethargy, nasal and ocular secretions, gauntness, coughing and combinations of these ailments. Therapy or treatments are then applied accordingly. Limitations of effectively determining clinical illness exist due to the severity of ailment. Duff and Galyean (2007) summarized that observable signs of illness, as described above, and a rectal temperature over 40^{o} C (104.0^{o} F) is indicative of BRD presence.

Pulmonary tissue lesions

Given increased knowledge about BRD, a gap exists between observations of illness and true infection. Wittum et al. (1996) observed 6-mo old calves (n = 469), that were monitored and treated for BRD from birth through harvest and concluded that 78% of cattle treated for BRD had pulmonary lesions evident at slaughter, whereas 68% of untreated steers also displayed pulmonary lesions at slaughter. Gardner et al. (1999) also observed the presence of lung lesions in 29% of non-treated Charolais steers (n = 222), that had been vaccinated with a modified live vaccine prior to feedlot entry and health evaluation. Similar observations were made by Schneider et al. (2009) where 60.6% of cattle never treated for illness had lung abrasions present, and 74% of cattle that were treated for illness also displayed lung tissue damage. These cattle (n = 1656), originated from 10 different herds from the midwest and southeast United States. The above described observations reflect the nature of subjective evaluations and the accuracy or inaccuracy of diagnosis of clinical illness by feedlot, or cattle health personnel. Table 2 summarizes additional published reports with lung lesion data.

Table 2. Comparisons of published reports for lung lesion data in feedlot cattle

Author/Study	n	Treated %	Treated for BRD, but no lesions	Not treated for BRD, but lesions present
Bryant et al. (1999)	439	17.0%	63.0%	42.0%
Buhman et al. (2000)	170	35.3%	NR	83.3%
Gardner et al. (1999)	222	50.0%	37.0%	29.0%
Schneider et al. (2009)	1665	8.17%	36.0%	60.6%
Thompson et al. (2006)	2036	22.6%	9.9%	38.4%
Wittum et al. (1996)	469	35.0%	22.0%	68.0%

It is important to note that previous illness status is not available prior to health monitoring system and treatment of the individual studies listed in Table 2. So it should be acknowledged that lung lesion causing morbidity could have occurred prior to trial observations. Given the high percentage of cattle that had lung lesions but were not treated for BRD, obvious limitations exist for diagnosis of illness based on visual signs of morbidity alone. The explanation for this high amount of subclinical illness is largely unknown, however, Noffsinger and Locatelli (2004) indicated this phenomenon may be related to predator/prey behavior as cattle may view feedlot or animal health personnel as predators, consequently hiding or masking visual signs of ailments to avoid drawing attention.

Bovine Respiratory Disease effects on feeding behavior

Clearly, detection of subclinical illness is challenging, and therefore estimates of the true prevalence of BRD can be easily misjudged. Aside from visual signs of morbidity, feed intake and feeding behavior have also been documented from healthy versus unhealthy cattle.

Hutcheson and Cole (1986) reported the averages of 18 experiments and overall 94.6% of "healthy" calves were observed eating as compared to 83.4% of calves classified as "morbid." Additionally, cattle identified as "morbid" had lower feed intake (as a percentage of body weight) by 0.9% as compared to healthy steers at 1.55% in the first 7 days after arrival. Using an electronic monitoring system, Buhman et al. (2000) observed lower frequency and duration of feed intake behavior in newly arrived feedlot cattle that were identified as sick on days 11 through 27 after arrival. On days 28 through 57 however, steers previously labeled as "sick" recorded higher frequency and duration of feeding as compared to their non-sick cohorts. Sick steers were identified using a scoring system that included a rectal temperature of greater the 40.0°C, visual signs of changes in attitude, cough, nasal secretion, ocular secretion, and hematologic examinations. Sowell et al. (1999) observed similar results in two, 32-day experiments where newly received cattle from various Texas sale barns were co-mingled, processed, and placed in one pen containing the GrowSafe® System. Cattle classified as healthy based on visual assessment from feedlot personnel had more bunk visits each day,

spending more time at those bunk visits as well. In trial 1, 57 of 108 steers were classified as morbid, and in trial 2, 117 of 143 calves were classified as morbid.

Bovine Respiratory Disease effects on weight gain

A reduction in weight gain was reported by Gardner et al. (1999) as they observed 1.47 kg/d for treated cattle and 1.53kg/day for untreated cattle using visual symptoms and rectal temperature greater than 40°C. Roeber et al. (2001) also observed similar response in cattle treated more than once having 0.25 kg/d reduction in average daily gain (ADG) as compared to cattle not being treated based on visual diagnosis of morbidity. Schneider et al. (2009) reported cattle that were treated for BRD, or had presence of lung lesions, had a 0.07 kg/d reduction in ADG as compared to non-treated cattle with no lung lesions.

Conflicting evidence exists in the literature for ADG response and BRD incidence. Wittum et al. (1996) found no difference in ADG between treated and untreated cattle, but concluded that 68% of untreated steers displayed pulmonary lesions at slaughter. Retrospective analyses in this experiment concluded that steers exhibiting lung lesions, regardless of treatment status, did have a 0.076 kg/d reduction in ADG as compared to cattle exhibiting no signs of lung lesions upon harvest.

Breed differences for Bovine Respiratory Disease occurrence

Incidence and morbidity of BRD has been recorded between breeds, although it has not been widely researched. Muggli-Cockett et al. (1992) reported Pinzgauer offspring had a higher incidence frequency for BRD postweaning (24.6%) compared to

the lowest incidence frequency (11.8%) in Angus herds from the Germ Plasm Utilization project where 10,142 cattle were evaluated from 1983 to 1988. Snowder et al. (2006) also evaluated MARC herd BRD data from 1987 to 2001, and observed that incidence frequency for BRD was highest for Pinzgauer, Braunvieh, Simmental, and Limousin at 35%, 34%, 33%, and 32%, respectively. Angus was the lowest at 10.2%, and the overall mean was 12.8% in the 12 breeds represented. Snowder et al. (2005) also reported MARC III composite (¼ Angus, ¼ Hereford, ¼ Pinzgauer, ¼ Red Poll) as not only having a lower incidence frequency of BRD at 9.7%, but also had one of the highest mortality rates at 17.2%. They concluded that some breeds or breed combinations are inherently more sensitive to BRD impacts and show more visual signs of BRD morbidity.

Mitigation of Bovine Respiratory Disease

Vaccinations have been shown to be an important solution for reducing the negative effects of many diseases. In terms of minimizing BRD occurrences, preventative methods have been heavily researched. Snowder et al. (2006) discussed practices that prevent pathogen introduction, limit exposure, and reduce transmission are all important steps upon entry into the feedlot. It is a common practice that BRD preventative protocols are applied based on the perceived risk assessment of a pen or lot of cattle received in commercial feedlot operations. Vaccines and other antimicrobials reduce incidence and severity of a disease outbreak, but are limited in terms of their ability to prevent and eradicate BRD entirely. A broad selection of commercial vaccines and antibiotic pharmaceuticals are available, however, none

include protection against all BRD pathogens (Perino, 1997). However, feedlot managers and animal health experts do perceive the use of pharmaceuticals as beneficial, as reflected by the National Animal Health Monitoring System (NAHMS). NAHMS (2013b; 2013c) reported that 96% of cattle in feedlots over 1,000 head capacity utilize a respiratory vaccine upon arrival and 26% of those same cattle are administered an antibiotic upon arrival as well. In feedyards of fewer than 1,000 head capacity 92.6% of the cattle received BRD vaccine but 31% were administered an antibiotic upon arrival.

Reducing the amount of stress incurred during the receiving period is important, especially for those cattle who are higher risk and more immune-compromised than others. Duff and Galyean, (2007) discussed that the benefits of metaphylaxis programs and prevention methods are attention worthy for susceptible cattle that are higher risk. In a review of preconditioning methods, Cole (1985) concluded that preconditioned animals had increased ADG on-farm and within the first 45 days of the feedlot period, and that morbidity and mortality rates were reduced by 23% and 0.7%, respectively, as compared to non-preconditioned contemporaries. More recent research has also supported these general findings as seen in Table 3.

Table 3. Comparisons of performance in preconditioned and non-preconditioned calves in the scientific literature

Author/Study	Preconditioned	Non-Preconditioned
Cravey (1996)		
Morbidity (cost per head)	$13.74	$30.66
Mortality	0.5%	2.6%
ADG	1.31, kg/day	1.17, kg/day
Roeber et al. (2001)		
Morbidity	35%	77%
Mortality	1.1%	11.4%
ADG	1.61, kg/day	1.69, kg/day
Lalman et al. (2005)		
Mobidity	7.0%	29.0%
Mortality	0.1%	3.0%
ADG	--	--

(As adopted from Mathis, 2008)

Health impacts on growth

The disciplines of growth, immunology, and beef cattle management have traditionally been studied and discussed with little reference to the complex nature of their over-lapping biological functions and associated variables. Gifford et al. (2012) summarized the impacts of immune response on physiological features that can lead to changes in growth. Following exposure of cattle to, and subsequent inflammation from, infection by viral and bacterial agents, the acute phase response occurs within 48 hours post infection. Stimulation of pro-inflammatory cytokines leads to fever, anorexia, muscle catabolism, and alters liver protein synthesis. Gifford et al. (2012) summarized that acute phase cytokines are highly expressed in damaged tissues

following immune response, and negatively affect the precursors to metabolism in human, mouse and swine models. In cattle, it is also hypothesized that a repartitioning of nutrients is directed toward immune response, and ultimately survival, instead of increasing skeletal muscle tissue growth.

Bovine Viral Diarrhea Virus

Since the focus of this research is the impact of Bovine Viral Diarrhea Virus (BVDV) on immune response and performance traits, this pathogen is now discussed in more detail. Aside from the losses of cattle at all phases of beef production, the other major threat of BVDV comes from persistently infected (PI) cattle. Calves persistently infected with BVDV result from vertical transmission of BVDV from the infected dam's bloodstream to her fetus during pregnancy (Larson et al., 2002).

Bovine Viral Diarrhea hinders beef cattle production on a substantial economic scale as the estimated cost of a single occurrence of PI in a beef cow herd has been estimated to range from $14.85 to $24.84 per cow annually (Larson et al., 2002). Hessman et al. (2009) observed growing cattle (n = 15,348), and economic analyses revealed performance losses were $88.26/animal due to exposure to PI calves; prevalence of PI cattle in this report was 0.04%. A similar observation was made by Loneragen et al. (2005), who reported the prevalence of PI cattle in commercial feedlots was 0.3%, and the presence of a single PI animal in a pen resulted in 43% increase of treatment for BRD.

Bovine Viral Diarrhea Virus persistent infection

It is important to note that the cause of PI calves is in-utero exposure between days 45 to 175 of pregnancy (Groom, 2004). Prior to development of the fetal immune system, PI calves fail to create an immune response to the BVD virus because they fail to distinguish the virus from itself, and these cattle subsequently serve as reservoirs of infection for other cattle (Chase et al., 2008). Because of a failure to respond to the infection, PI cattle continuously shed BVD virus through horizontal transmission from one animal to others through mucosal secretions (Larson et al., 2002). Wittem et al. (2001) reported estimates of 18.5% of PI calves decease at or before weaning. Estimates by Loneragan et al. (2005) indicate that 33% of PI cattle will live through the finishing process of beef production systems and be harvested with their non-PI contemporaries. Larson et al. (2004) estimated similar figures of 17% to 40% of PI cattle can reach puberty and breeding ages. Ultimately, these figures represent an elevated exposure of non-infected cattle to BVDV in all production phases.

Bovine Viral Diarrhea Virus classifications

Bovine Viral Diarrhea virus can be classified into 2 genotypes (BVD type 1 and BVD type 2). Beyond these distinctions, each genotype occupies several subtypes such as BVD1a, BVD1b, BVD1c, etc; BVD1b being the most prevailing subtype in U.S. feedlots, whereas BVD1d is the most common in subtype in the Australian cattle industries (Fulton et al., 2003b; 2009). Beyond these genotype separations, different BVD biotypes exist. The biotype is defined as cytopathic (CP) or non-cytopathic (NCP)

(Ahn et al., 2005). These biotypes are classified based on the presence or absence of visible cytopathic, degenerative or degrading, effects in infected cell cultures. Observation by Ahn et al. (2005) recorded differences in occurrence of biotypes for BVDV such that 30% of samples were defined as CP and 70% were classified NCP. Fulton et al. (2000b) reported similar figures in vaccinated and non- vaccinated steers with 20.8% of collected samples being CP and 79.2% of samples NCP.

Bovine Viral Diarrhea Virus clinical symptoms

Clinical symptoms of BVDV as reviewed by Peterhans et al. (2003) and Fulton et al. (2003a) include those similar to other respiratory infections. Further, the virus can affect the digestive tract, fetal development, and the immune system in addition to causing mucosal disease. Bovine Viral Diarrhea virus has a dual nature for infection; BVDV itself serves as an infectious agent itself, but it also serves as an immune-suppressor of health defenses (Baker, 1995). With defense mechanisms suppressed, secondary bacterial colonization occurs which commonly leads to subsidiary infections (Edwards et al., 1986).

Bovine Viral Diarrhea Virus laboratory diagnosis

In terms of handling the occurrences of BVD, an important aspect is accurate screening and diagnosis of PI calves. Sandvik (2005) described in detail numerous methods of laboratory testing for BVD virus itself, by through virus isolations, or by immune function response to BVD, through virus neutralizing antibodies. Cornish et al. (2005) summarized important characteristics of laboratory testing for detecting PI

calves to have large capacity, be economical, accurate, and timely in order to be suitable for practical application.

Immune system considerations

Immunity is the ability to resist disease or infection from foreign substances that threaten wellbeing, and the nature of the immune system is very complex. Two segments of immune function exist, referred to as innate and adaptive. The innate system includes non-specific response mechanisms, and the adaptive immune system is antigen specific and involves immunological memory (Abbas and Lichtman, 2007). The principal components of innate immunity are (1) physical and chemical barriers, such as epithelia and antimicrobial substances produced at epithelial surfaces; (2) phagocytic cells (neutrophils, macrophages) and natural killer (NK) cells; (3) blood proteins, including members of the complement system and other mediators of inflammation; and (4) cytokine proteins that regulate and coordinate many of the activities of the cells of innate immunity.

The mechanisms of innate immunity are specific for structures that are common to groups of related microbes and may not distinguish fine differences between foreign substances. Innate immunity provides the initial lines of defense against foreign microbes (Abbas and Lichtman, 2007). Conversely, the adaptive immune system has the capacity to distinguish among different, even closely related microbes and molecules, and for this reason is also called specific immunity (Abbas and Lichtman, 2007).

Two types of adaptive immune responses, humoral and cell-mediated, can also be considered. Cell-mediated immunity is derived from different components of the immune system and functions to eliminate different types of microbes. Humoral immunity is mediated by antibodies in the blood and mucosal secretions and produced by B lymphocytes (B-cells). Cell-mediated immunity, also called cellular immunity, is mediated by T lymphocytes (T-cells). Intracellular microbes, such as viruses and some bacteria, survive and proliferate inside phagocytes and other host cells, where they are inaccessible to circulating antibodies. Defense against such infections is a function of cell-mediated immunity, promoting the destruction of microbes residing in phagocytes or the killing of infected cells to eliminate reservoirs of infection (Abbas and Lichtman, 2007).

Protective immunity against a microbe may be induced by the host's response to the microbe or by the transfer of antibodies or lymphocytes specific for the microbe. The form of immunity that is induced by exposure to a foreign antigen is called active immunity because the immunized individual plays an active role in responding to the antigen (Abbas and Lichtman, 2007). Immunity can also be conferred on an individual by transferring serum or lymphocytes from a specifically immunized individual. The recipient of such a transfer becomes immune to the particular antigen without ever having been exposed to or having responded to that antigen. Therefore, this form of immunity is called passive immunity (Abbas and Lichtman, 2007), and is the primary

mechanism by which cows provide immunity to their calves through colostrum, as very little to no passive transfer occurs across the placenta in cattle.

Vaccine products generally contain modified-live (MLV) or killed viruses and bacteria toxins known to cause diseases. These products are administered to induce the body's immune system into creating antibodies and develop immunological memory (Faries, 1999). Adjuvants are also included in available vaccines to slow the release of the antigen into the system to extend the immune response; adjuvants also elicit an innate response.

Historically, most killed vaccine adjuvants have been comprised of aluminum hydroxide or oil and water combinations (Roth and Hednerson, 2001). Vaccines can contain an assortment of biological agents such as inactive toxins (known as toxoids), killed bacteria (known as bacterins) and combinations of adjuvants which elevate the level of effectiveness of the antigens (Faries, 1999). Faries (1999) also summarized that vaccines are identified as either infectious or noninfectious. Infectious vaccines contain an organism that is modified or altered to reduce its virulence so that it will not cause disease, but will still be infectious enough to provide immunity. Modified live vaccines are infectious vaccines that achieve a desired level of infection. Immunity of the animal prevents the establishment of disease and provides immunity. Noninfectious vaccines are unable to infect or replicate infectious agents. Generally, noninfectious vaccines are weaker in their ability to illicit an immune response, so a second dose, or booster, is required 2-4 weeks later. The initial dose of vaccine is a priming-sensitizing dose that

provides little to no protection and the booster provides protection for 6 to 12 months (Faries, 1999).

Protective immunity against viruses from vaccination

There appear to be some discrepancies among reports pertaining to the effectiveness and duration of protection that vaccines provide for BVD. Cortese et al. (1998) concluded that vaccination with a MLV BVD Type 1 triggered antibodies to numerous strains of both BVD type 1 and BVD type 2 virus strains that were detectable 18 months post vaccination. Fulton et al. (1995) indicated a decline in BVD antibody titers by day 140 following vaccination. Step et al. (2009) showed that single and multiple vaccinations of BVDV prevented disease incidence prior to PI exposure. Furthermore, in an evaluation of the effect of PI-BVDV exposure to non-exposed cattle, Booker et al. (2008) concluded that pens containing animals PI with BVDV type 1 had more BRD treatments and mortalities, but calves PI with BVDV type 2 had no effect on the health of non-exposed calves. These conflicting results in the literature may be because of the type of virus present in the PI animals. There are thousands of strains of BVDV with widely varying levels of morbidity incidence (Ridpath et al., 2007).

Some vaccines that target specific antigens, such as toxoid vaccines, are meant to completely prevent disease from infection, whereas vaccines formulated for more complex agents of disease that tend to have more numerous antigenic strains are less likely to produce a complete prevention level of protection (Faries, 1999). Callan and Garry (2002) summarized respiratory vaccines as disease modifiers rather than absolute

preventative agents. Additional benefits of vaccination exist which not only protects vaccinated individuals, but also reduces the ability to shed infections to pen mates or newly arrived comingled calves (Frank et al., 2003).

Viruses use two different strategies to infect hosts. Peterhans (2003) reviewed that a virus may either cause a persistent infection in individual animals to infect new hosts, or, viruses can also use the 'hit-and-run" strategy which is a short duration, transient infection followed by a rapid transfer to a different host and continued replication in other animals.

Virulence of BVDV has been characterized as having a broad range of effects based upon the amount of infection or severity of infection induced (Ridpath et al., 2007). Liebler-Tenorio et al. (2003) observed differences in clinical observations and rectal temperature changes in colostrum deprived, non-vaccinated steers less than 4 months of age when challenged with 2 different BVDV type 2 strains. Observations were made following an intranasal challenge of a naturally occurring low virulent strain, or a highly virulent strain isolated from a severe field outbreak. Calves receiving the low virulent strain expressed a mildly elevated body temperature at day 7 following challenge with no changes in feed intake or observable behavior differences. Conversely, calves inoculated with the highly virulent strain exhibited elevated body temperature (> 40^{o}C) shortly following challenge which persisted for several days. Calves in the high virulence group also became lethargic and apathetic in behavior. Similar findings were made by Kelling et al. (2002) where 5 different isolates of BVDV

type II (2 highly virulent strains and 2 lowly virulent strains) were experimentally induced into 6 to 9 month old crossbred calves. Kelling et al. (2002) observed that calves inoculated with high-virulence strains developed more signs of respiratory tract disease, displayed elevated rectal temperature 6 days following inoculation, and exhibited more lethargic demeanor as compared to calves challenged with low-virulent strains.

The variation in virulence presents challenges from a research standpoint. Efficacy of vaccine and vaccine use protocol studies in the field have been limited by the lack of repeatability and under-developed accepted criteria for appropriate research models. Traditionally, results from studies using BVDV type 2 have been readily available; however results from BVDV type 1 challenges are less common. One such BVDV1 strain that has been used in vaccines as well as a popular challenge strain is BVDV NY-1. Isolated from a field case in New York, calves infected with BVDV NY-1 were reported to respond with symptoms of pyrexia, reduction in white blood cells, diarrhea, reduced appetite, depression, and reddening of the gums (Baker et al., 1954). Ridpath et al. (2007) summarized two problems in using BVDV NY-1 when conducting viral challenges: (1) that clinical presentation of infection was reported as mild in comparison to BVDV strains R5013, R2360, and CA0401186A, and (2) the conflicting results in vaccine efficacy in studies using BVDV NY-1 in the treatment vaccine as well as the challenge virus simultaneously.

One of the aforementioned BVDV strains used by Ridpath et al. (2007) that compared BVDV NY-1 to other field strains was used in this research project. Bovine Viral Diarrhea Virus CA0401186A was discovered from a PI calf in California that was one of 24 calves with brain and skeletal deformities born to heifers in a single herd. Tissues containing CA0401186a were submitted to the USDA-ARS National Animal Disease Center in Ames, IA from the Tulare Laboratory of the California Animal Health and Food Safety Laboratory. It was characterized as a noncytopathic biotype and found to be of the BVDV1b subgenotype (Ridpath et al., 2007).

Wilson (1989) defined the efficacy of a vaccine as its ability to reduce the overall level of respiratory disease. With this broad definition, a limited amount of literature exists pertaining to positive results for the efficacy of vaccination strategies in field trials. Reasons for this limitation were summarized by Wilson (1989) in that the methods of identifying respiratory disease are often based on clinical observation only. Variables including severity of illness and length of illness are un-detected. Finally, differences of repeatability issues which are unavailable in field studies as compared to laboratory evaluations (Wilson, 1989).

Considering the complex characteristics of BVDV, there is also complexity in BVDV vaccination strategies. Fulton et al. (2002) observed that BVDV was an important contributing factor to BRD in 2 studies, with BVDV subtype 1b being the most predominant. Fulton et al. (2002) and Fulton et al. (2005) also briefly reviewed popular BRD vaccines containing BVDV, and summarized that only a small number of

commercially available vaccines actually contained BVDV 1b antigenic material. A problem with this strategy is that even though cattle are vaccinated with BVDV 1a or 2, they may still be susceptible to the most common BVDV subtype, 1b. Fulton et al. (2005) concluded that vaccination with a MLV vaccine containing BVDV subtypes 1a and 2 did not prevent infection in vaccinated calves when exposed to PI calves with BVDV1b. Fulton et al. (2003b) also reported that vaccines containing BVDV1a induce lower antibodies to BVDV1b than to BVDV1a in 3 separate USDA licensed vaccines.

Summary of literature review

Bovine Respiratory Disease Complex remains widespread in beef cattle production systems. Morbidity and mortality resulting from exposure to viral and bacterial infections that work in concert to activate immune responses. Changes in feed intake and feeding behavior in feedlot cattle have been observed due to BRD infections. Subclinical infection of BRD is a major hindrance of illness diagnosis for feedlot personnel as evidence of infection has been observed in pulmonary tissues, yet no visual signs that would warrant treatment were recorded. Breed types and combinations of breeds have also been linked to a lower incidence of BRD as well. One major component of BRD is Bovine Viral Diarrhea Virus. One of the reasons BVDV draws much attention is due to unidentified PI calves that are a major source of spreading infection. Even in events of immunization, exposure to varying subtypes of BVDV can still result in infection leaving questionable results of vaccine efficacy. Thus, research is needed that addresses the genetic influences related to health, immune

responses and animal performance in cattle exposed to BVDV. The long-term goal of this research is to investigate the genomic aspects of health related characterizations and as a preliminary component of the long-term goal, the objective for this dissertation is to investigate phenotypes associated with traditional production measures of feed intake, feeding frequency, growth performance, and morbidity aspects of *Bos indicus* crossbred steers of known genetic background following BRD vaccination and BVDV challenge. To satisfy the overall goal, specific approaches evaluated: (1) the effects of (a) vaccine type, (b) sire groups and (c) elevated rectal temperature status (above 40^{o}C for 14 days post challenge) on daily feed intake, bunk visit frequency, and average daily weight gain, and (2) the relationships of clinical morbidity signs and lung color scores at slaughter with daily feed intake, bunk visit frequency, and average daily gain as well as their distributions across (a) vaccine type, (b) sire groups and (c) rectal temperature status. Interactions involving vaccine type, sire group and rectal temperature status were of particular interest to be investigated.

MATERIALS AND METHODS

Animal procedures

Half-blood (F_2 and F_3) Angus-Nelore steers from the Texas A&M University McGregor Genomics herd were utilized. This herd represents a unique population of *Bos taurus-Bos indicus* crossbred cattle that are used to identify regions of the genome that are related to production traits of economic relevance. The steers for this project were spring-born and not vaccinated against BRD pathogens as calves. Steers were confirmed to be free of BVDV-PI prior to vaccination, and absence of PI was confirmed through evaluation of ear notch samples by antigen capture ELISA at the Texas Veterinary Medical Diagnostic Laboratory (TVMDL, Amarillo, TX). All animal procedures were reviewed and approved by the Texas A&M University Institutional Animal Care and Use Committee (AUP# 2010-080 and 2013-0069) as well as the Texas A&M University Institutional Biosafety Committee.

Steers were stratified by sire and genomics cow family across 3 vaccine treatment groups of killed vaccine (KV), modified-live (MLV), and non-vaccinated (NON). Table 4 shows the number of observations across vaccine groups and years of study.

Table 4. Number of cattle in each vaccine type group per year

Vaccine type	2010 (n = 78)	2011 (n = 104)	2012 (n = 106)	2013 (n = 95)
Killed vaccine (KV)	n = 28	n = 34	n = 35	n = 31
Modified-live vaccine (MLV)	n = 25	n = 35	n = 35	n = 33
Non-vaccinated (NON)	n = 25	n = 35	n = 36	n = 31

Steers in the KV group received initial Vira-shield® (Novartis Animal Health US, Inc.) vaccine on day -56 or -49 and a booster dose on day -35, -28, or -25, depending on year, but with a target of 21 days between priming and booster vaccinations. Steers in the MLV group were vaccinated with Arsenal 4.1® (Novartis Animal Health US, Inc.) on day -35, -28, or -25, depending on year, prior to the challenge. The steers of the NON group remained as non-vaccinated. Steers receiving the MLV vaccine were kept separate from KV and NON steers for 7 to 10 days depending upon the year. The dates for vaccinations and data collections across years are summarized in Table 5.

Table 5. Dates for procedures and associated day of trial across years

	2010		2011		2012		2013	
Procedure	Date	Day	Date	Day	Date	Day	Date	Day
KV I[1]	3/16	-56	3/22	-49	3/27	-49	4/16	-49
KV II/MLV[1]	4/6	-35	4/15	-25	4/17	-28	5/14	-28
Challenge	5/11	0	5/10	0	5/15	0	6/4	0
Collect Data	5/12	1	--	--	--	--	--	--
Collect Data	5/14	3	5/13	3	5/18	3	6/7	3
Collect Data	5/18	7	5/17	7	5/22	7	6/11	7
Collect Data	5/21	10	5/20	10	5/25	10	6/14	10
Collect Data	5/25	14	5/24	14	5/29	14	6/18	14
Collect Data	6/8	28	6/7	28	6/12	28	7/2	28
Collect Data	6/22	42	6/21	42	6/26	42	7/16	42

[1]KV = killed vaccine, MLV = modified live vaccine. After 2010 it was decided not to collect weight or rectal temps on animals the day following challenge.

On day 0, steers were challenged with a type 1b non-cytopathic BVDV strain (CA0401186a) obtained from the USDA-ARS National Animal Disease Center (NADC) (Ridpath et al., 2007). This strain was isolated from a PI calf and submitted to the NADC from the California Animal Health and Food Safety Laboratory in Tulare. Each steer received 5 mL of inoculum (1×10^5 TCID/mL). A 2.5 mL dose was placed in each nasal passage; the animal's nose was then elevated until it was visually observed that the steer had swallowed to confirm challenge virus solution was ingested. This particular strain of BVDV was chosen for this study because it had previously been reported to

cause recognized immunological and clinical signs of morbidity, but without risk of extreme illness or death (Ridpath et al., 2007).

Cattle were fed a high-forage growing diet that consisted of approximately 31.5% corn, 36.5% chopped alfalfa hay, 24.5% dry distillers grains, 2.5% commercial premix, and 5% molasses. Cattle were housed and fed at the Texas A&M University Beef Systems Research Unit in College Station, Texas where 4 pens are equipped with a GrowSafe® feed intake monitoring system. Cattle were housed so that the treatment groups were stratified across the 4 pens with approximately 20 to 26 steers per pen depending on the year. Cattle were acclimated to the diet for 6 to 10 weeks prior to the challenge day in each year; however, individual intake was not accessed until after isolation of steers following MLV administration at which time they were placed into the pens they remained in until 42 days post-challenge.

Following the 42-day post-challenge evaluation period, cattle were transported to a commercial feedlot and fed for approximately 150 to 180 days, then harvested at a commercial processing plant. At harvest, lungs and livers of animals were evaluated for presence of lesions and lung color score by the same evaluator in all years. Table 6 explains the lung color score system description.

Table 6. Lung coloration and adhesion scores

Score	Description
1	Pink healthy lung
2	Less than 25% discoloration
3	More than 25% but less than 50% discoloration
4	More than 50% but less than 75% discoloration
5	More than 75% discoloration

Sample and data collection

Body weights were measured and rectal temperatures were evaluated via digital rectal thermometer on days 0, 3, 7, 10, 14, 28, and 42 following viral challenge. Average daily gain (ADG) was calculated from days 0 through 42 as well as three periods: period 1 (days 0 to 14), period 2 (days 14 to 28), and period 3 (days 28 to 42).

Clinical observations were conducted twice daily for 14 days following challenge to assess apparent health symptoms with a score of 0 (no symptoms), or 1 to 5 (least severe to most severe) for commonly associated symptoms of BRD/BVD (cough, ocular secretion, nasal secretion, depression, diarrhea, and gauntness/shrink). From days 15 to 42 observations were conducted once daily. Animals exhibiting rectal temperatures over 40^{o}C were administered a commercially available antimicrobial approved for cattle and dosed per label directions.

Statistical analyses

Mixed model procedures of SAS (SAS Inst. Inc., Cary, NC), were used for analyses of daily feed intake (DFI) and daily feeding frequency with a model that includes fixed effects of vaccine type, year, day(nested within year), sire, pen(nested within year), high rectal temperature status days 3 to 14 (yes or no), two-factor interactions of sire × vaccine type, and three-factor interaction of vaccine type × day × high rectal temperature status days 3 to 14 (yes or no). Rectal temperature measurements were analyzed with a model that included day nested within year, pen nested within year, year, vaccine type, sire, and two-way interactions of day × vaccine type, and day × sire. Analyses of weight measurements included a model with day nested within year, pen nested within year, year, vaccine type, sire, and day × sire interaction. These models were analyzed as repeated measures with a first order autoregressive covariance structure.

Average daily gain calculated for the three 14-d periods as well as the 42-day period was analyzed with a model containing fixed effects of pen nested within year, vaccine type, sire, high rectal temperature status days 3 to 14 (yes or no), day 0 weight as a covariate, and two-way interactions or vaccine type × high rectal temperature status days 3 to 14 (yes or no), sire × high rectal temperature status days 3 to 14 (yes or no).

Twenty-three steers representing 12 different sires were removed from analyses due to limited sire group size, which prevented appropriate stratification

assignment across the three vaccine types. Least squares means were compared for effects that produced a significant F-test ($P \leq 0.05$) with two-tailed *t*-tests.

Frequency distributions of threshold rectal temperature status, visual morbidity sign status and lung color scores across other study factors such as vaccine type, pen and year were also evaluated, and Chi-square tests were examined.

RESULTS AND DISCUSSION

A general summary of the traits analyzed through repeated measures is presented in Table 7. There was considerable individual variation for all traits.

Table 7. Summary statistics for variables investigated

Variable	Mean	SD	CV	Minimum	Maximum
Weight, kg	344.1	51.6	15.0	188.7	526.1
Rectal temperature, ^{o}C	39.8	0.52	1.3	37.8	42.3
Daily feed bunk visit frequency, visits/animal/day	70	27	38.6	1	207
Daily feed intake, kg	10.7	2.7	25.2	0.0	21.0
ADG days 0 to 14, kg	0.66	0.7	106.1	-1.88	3.05
ADG days 14 to 28, kg	1.57	0.6	38.2	-1.62	3.24
ADG days 28 to 42, kg	1.23	0.49	39.8	-0.65	3.05
ADG days 0 to 42, kg	1.16	0.34	29.3	-0.43	1.90

Significance of the fixed effects for weight and rectal temperature analyses are shown in Table 8. Day within year, year, and sire were important sources of variation for both of these traits. Differences were also observed for vaccine type and the day × vaccine type interaction for rectal temperature; the day × vaccine type interaction approached significance for weight.

Table 8. Significance levels (*P*-values) for effects in the weight and rectal temperature models

Effect	Weight	Rectal temperature
Day(Year)	< 0.001	< 0.001
Pen(Year)	0.285	0.002
Year	< 0.001	< 0.001
Vaccine type	0.239	0.040
Sire	< 0.001	< 0.001
Day × Vaccine type	0.091	< 0.001
Day × Sire	--	0.148

Table 9 shows the levels of significance for the effects included in models for daily feed intake and daily feed bunk visits. Day within year, pen within year, year, sire, the two-way sire by vaccine type interaction, and the three-way day by vaccine type by rectal temperature threshold status interaction influenced ($P < 0.001$) both of these traits.

Table 9. Significance levels (*P*-values) for effects in the daily feed intake and daily bunk visit frequency models

Effect	Daily feed intake	Daily bunk visit frequency
Day(Year)	< 0.001	< 0.001
Pen(Year)	< 0.001	< 0.001
Year	< 0.001	< 0.001
Vaccine type	.388	.646
Sire	< 0.001	< 0.001
Sire × Vaccine type	0.001	< 0.001
Day × Vaccine type × High rectal temperature status over 40^{o}C	< 0.001	< 0.001

Significance levels for effects included in the ADG models are provided in Table 10 and are presented for the total 42-day period post-challenge as well as for 14-day intervals. Pen within year, year, and the regression on day-0 weight were typically significant effects with the exceptions being no year effect for ADG during the last 14 days, and no significant effect of day-0 weight during the first 14 days post challenge. Sire was only significant for ADG during the second 14-day period; rectal temperature status was important for the first and third 14-day periods, but not during the second period or overall 42-day period. The same models were used for all ADG periods. A vaccine type × rectal temperature status interaction was seen for ADG only in the second 14-day period, and there was a tendency for a sire × rectal temperature status interaction ($P = 0.09$) for ADG during the third period.

Table 10. Significance levels (*P*-values) of effects for the average daily gain models

	ADG			
Effect	Days 0 to 42	Days 0 to 14	Days 14 to 28	Days 28 to 42
Pen(Year)	.002	.003	< 0.001	0.004
Year	< 0.001	< 0.001	< 0.001	.161
Day 0 weight	< 0.001	.415	< 0.001	0.004
Vaccine type	.102	.080	0.773	0.165
Sire	.139	.483	0.055	0.133
High rectal temperature status over 40°C	.386	.022	0.331	0.023
Vaccine type × High rectal temperature status over 40°C	.161	.955	< 0.001	0.352
Sire × High rectal temperature status over 40°C	.253	.657	0.230	0.087

Weight analyses

Initially, it was not the intent to include year as a fixed effect in any analyses. Following preliminary evaluation it was concluded that including nested effects of day(year), pen(year) and year itself was the most appropriate method. This method allowed for evaluation of the year-to-year variation, some of which is due to imbalance of sires across years. Figure 1 displays the weights for the effect of day within year. Day 0 for years 2010 to 2013 was May 11, May 10, May 15, and June 4, respectively. Day 0 was delayed in 2013 to prevent potential issues with other cattle being treated for BRD in the same facilities in May; as a result cattle in 2013 were approximately two weeks older on day 0 than in previous years. Steers in the 2012 trial were managed with a growing diet following weaning as compared to the steers in 2010 and 2011 trials which were managed in a grazing with supplementation program. These management differences, post weaning, helps explain the differences for weight at day 0 of the 2012 steers as compared to 2010 and 2011 steers.

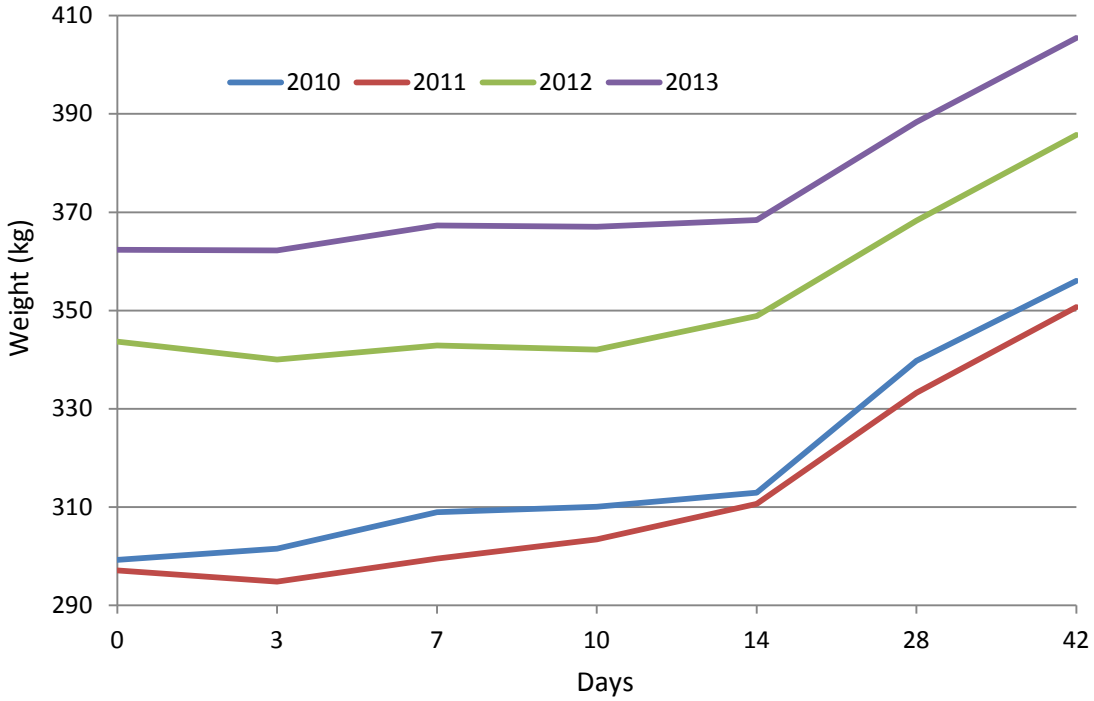

Figure 1. Least squares means for weight on evaluation days within year

Sire group was a source of variation for overall weight with means provided in Figure 2. Sires 297J and 482T were significantly higher for weight over 158U, 229T, 497S, 673S, 7152, 7238, 7530, 8048, 8154, 8213, and 8428. Sires 673S and 497S were the lowest ranking for weight. The sire 673S was different from 12 others, but not different from 158U, 422T, 497S, 673S, 7152, 7238, 7530, and 8428. Sire group 230T, 422T, 461T, 494S, 539S, and 8154 were intermediate and only different from a few other sire groups. It was of interest to evaluate differences in weights among sire groups and compare the results to those of other traits that might be weight-influenced.

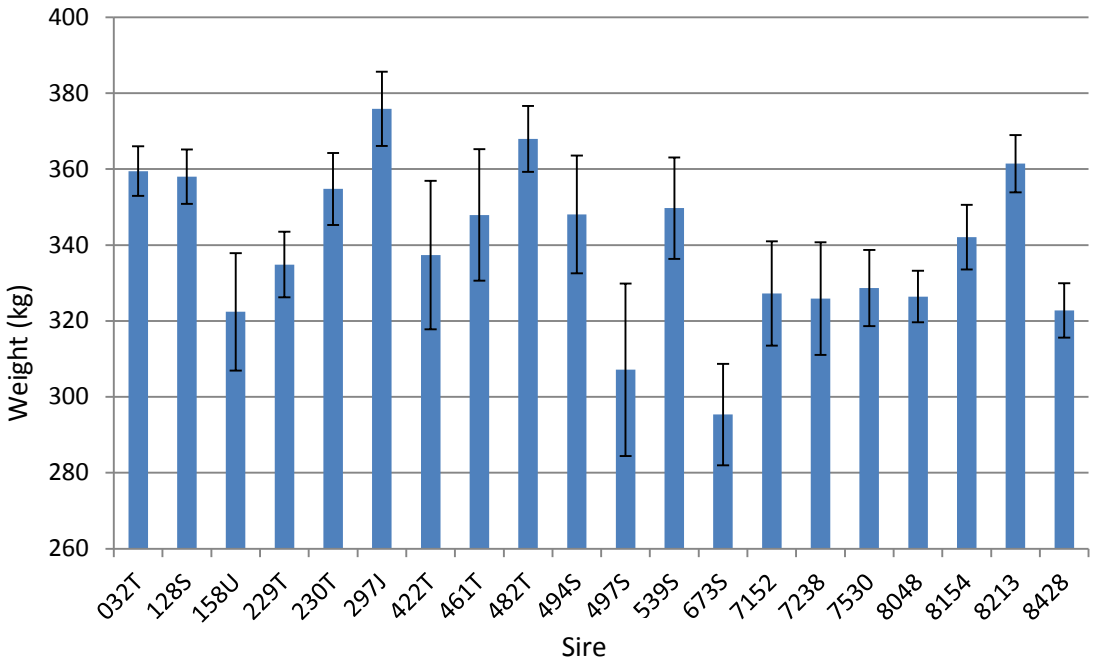

Figure 2. Least squares means of weight by sire groups.

Although not significant at the $P \leq 0.05$ level, the interaction of vaccine type × day on weight approached significance ($P = 0.09$), and the least squares means for these combinations are displayed in Figure 3. Overall 3 years, the MLV and NON vaccinated steers were very similar for weight, but KV steers tended to be lower at each observation point, and the explanation for this is unclear.

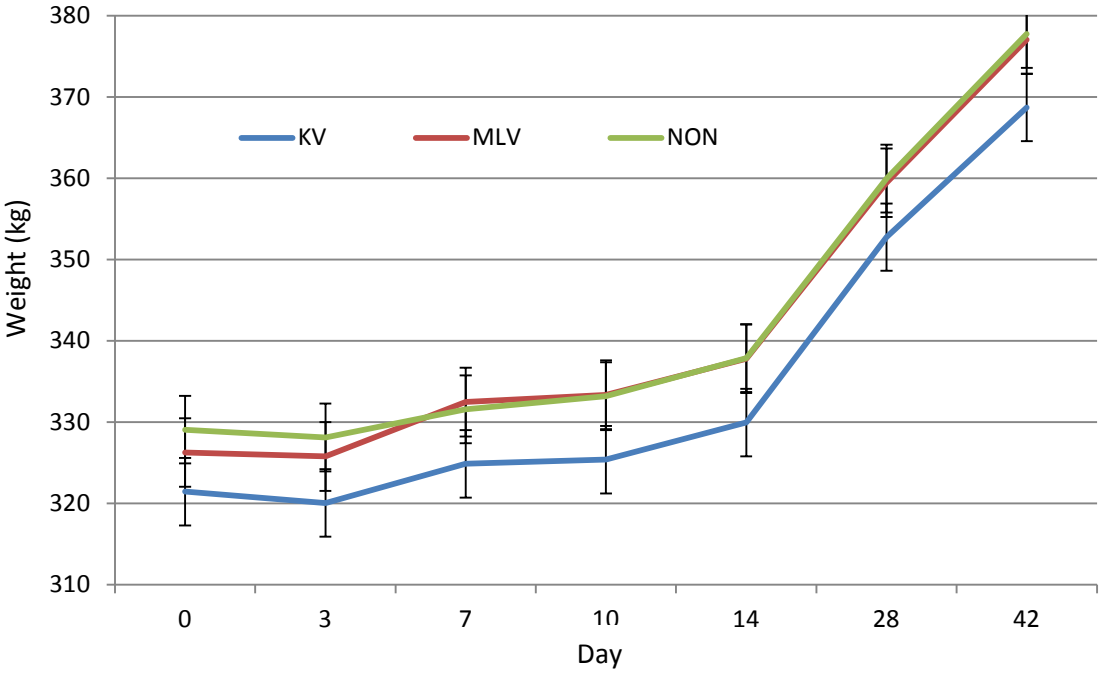

Figure 3. Least squares means of weight for vaccine type by day following challenge. KV = Killed, MLV = modified live, NON = non-vaccinated.

Rectal temperature analyses

A similar pattern for rectal temperatures was observed for 2010 and 2011 across the seven collection times as they decreased from day 3 through 10 then became gradually higher through days 14 through 42 (Figure 4). The least amount of change over the collection days was observed in the 2013 trial as no differences across days were significant. The 2012 rectal temperature observations increased from day 0 through 7, dropped significantly lower at day 10, and then increased at day 14 through 42.

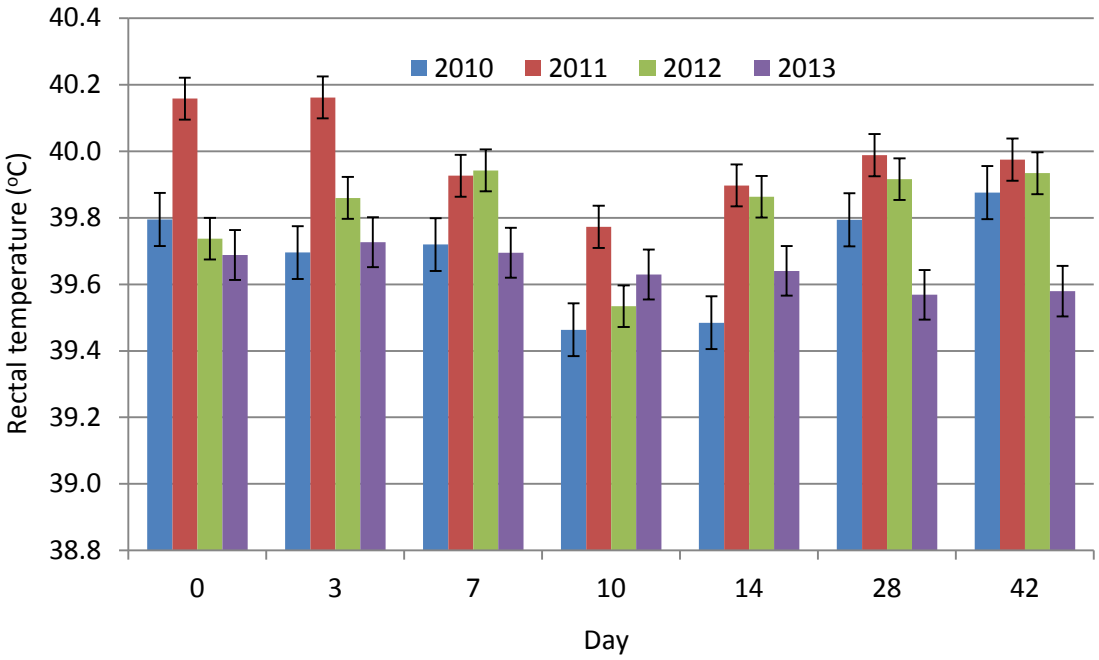

Figure 4. Least squares means of rectal temperature for day within year

When considering rectal temperature differences due to vaccine type, the KV vaccine group and NON vaccine group were higher ($P \leq 0.05$) than the MLV vaccine group across all years (Figure 5.). No differences were observed between the KV and NON vaccine groups across years.

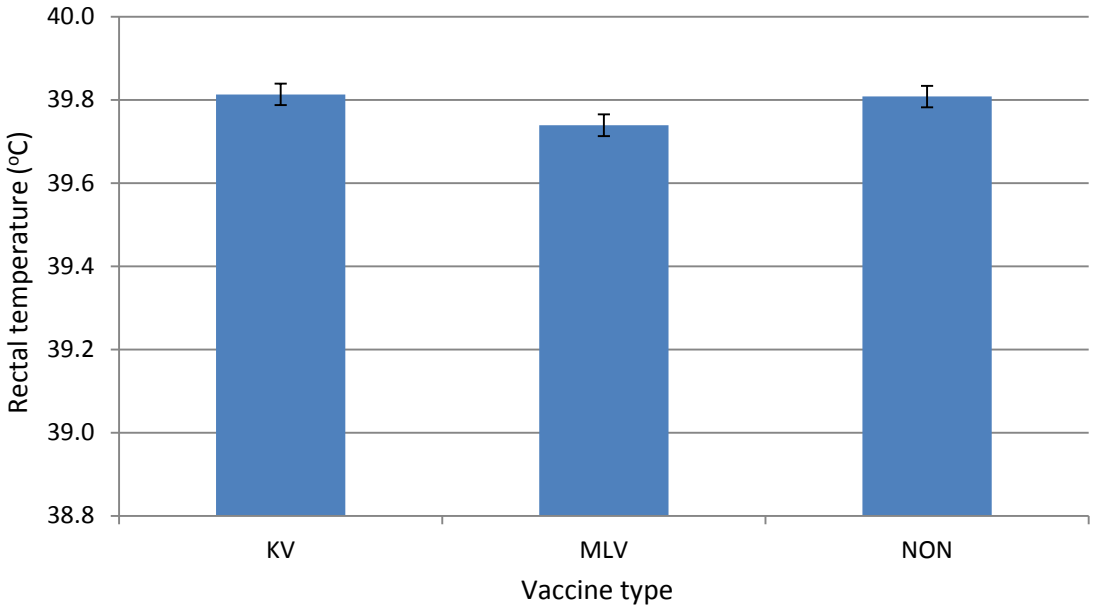

Figure 5. Least squares means of rectal temperature by vaccine type.
KV = Killed, MLV = modified live, NON = non-vaccinated.

Due to the MLV vaccinated steers having lower rectal temperature across all years, it was not surprising that a smaller proportion of MLV steers had rectal temperatures that reached above the 40.0°C threshold established for therapeutic treatment; 47.5% of the MLV steers exhibited high rectal temperature status as compared to 67.2% of the KV and NON steers. Table 11 shows the distributions of the steers from known sires across vaccine types.

Table 11. Distribution of high rectal temperature status over 40°C across vaccine type

Vaccine type	Rectal temperature threshold status: NO	YES	Total
Killed (KV)	39 32.8% of KV row 27.7% of NO column	80 67.2% of KV row 36.7% of YES column	119
Modified live (MLV)	62 52.5% of MLV row 44.0% of NO column	56 47.5% of MLV row 25.7% of YES column	118
Non-vaccinated (NON)	40 32.8% of NON row 28.4% of NO column	82 67.2% of NON row 37.6% of YES column	122
Total[1]	141	218	359

[1]Relative to number of steers with sire known. Distributions different (*P* = 0.001) across vaccine types based on Chi-square test.

Rectal temperature status distribution for all steers in the project is displayed in Table 12. Chi-square tests were used to analyze the distributions of rectal temperature status across other categorical study factors. The single significant Chi-square result was related to vaccine type where 47.2% of the MLV steers were above the rectal temperature threshold, but the KV and NON steers had 66.1% and 67.5%, respectively, above the threshold. Because the rectal temperature threshold of 40.0°C was the factor that dictated administration of BRD antibiotic treatment in this trial, this rectal temperature status was also evaluated as to its impact on other traits.

Table 12. Distributions of animals for threshold rectal temperature category in the 14-day period following challenge across other study factors[1]

	Year of trial			
	2010	2011	2012	2013
Below	43 (55.1%)	29 (27.9%)	41 (39.1%)	38 (40.9%)
Above	35 (44.9%)	75 (72.1%)	64 (60.9%)	55 (59.1%)
Total	78	104	105	93

	Vaccine type		
	KV	MLV	NON
Below	43 (33.9%)	67 (52.8%)	41 (32.5%)
Above	84 (66.1%)	60 (47.2%)	85 (67.5%)
Total	127	127	126

	Feedlot pen			
	1	2	3	4
Below	34 (35.8%)	34 (35.4%)	37 (39.0%)	46 (48.9%)
Above	61 (64.2%)	62 (64.6%)	58 (61.0%)	48 (51.1%)
Total	95	96	95	94

	Evidence of visual morbidity signs	
	No	Yes
Below	132 (40.4%)	19 (35.9%)
Above	195 (59.6%)	34 (64.2%)
Total	327	53

[1]Relative to all cattle in trial (n = 380).

Significant differences for rectal temperature were observed due to sire (Figure 6). Sire groups 032T, 297J, 230T, 8428, and 7152 were not different from each other but exhibited lower ($P \leq 0.05$) rectal temperatures than 8 of the 20 sire groups represented. Conversely, calves in sire groups 7238, 422T, 8213, 158U, 539S, 8048, were higher than sire groups 032T, 297J, 230T, 8428, and 7152, but not different from the remaining 9 sire groups. Sires 7238 and 8213 were higher ($P \leq 0.05$) than 10 of the

20 sire groups; sires 422T, 158U, 539S, 497S, 8048, 494S, 482T, 673S, 128S, 7530, 229T, 8154, 461T did not differ from each other. When looking at the rankings of sire groups for rectal temperature and weight, there was no similar pattern.

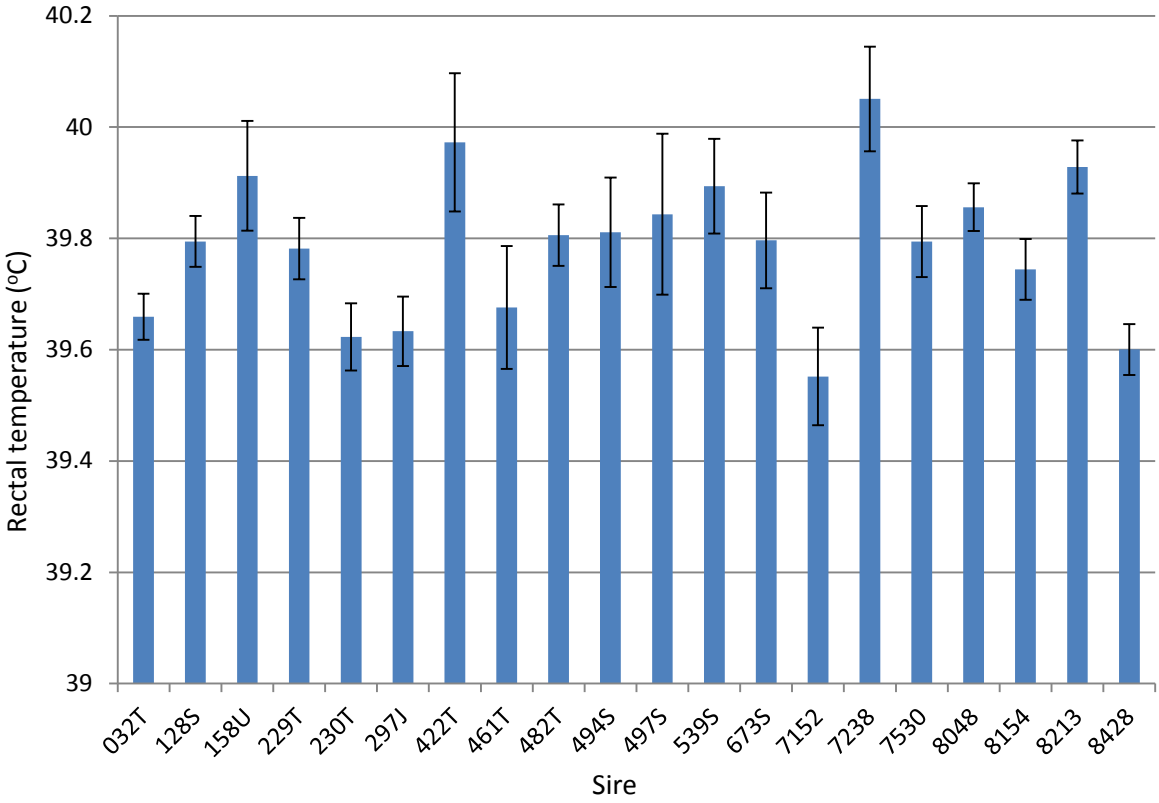

Figure 6. Least squares means of rectal temperature by sire groups

Least squares means of rectal temperature for the vaccine type × day interaction are provided in Figure 7. The non-vaccinated steers exhibited the highest amount of fluctuation across observation days. At day 3 the non-vaccinated steers recorded the highest rectal temperatures (with a least squares means estimate over

40.0^{o}C) which was higher ($P \leq 0.05$) than all other observations except for KV steers on days 3 and 7. Day 10 for the NON vaccine group was significantly lower than the other days in this group while days 0, 7, 28, and 42 were not different. Within the MLV group, days 0 and 28 ranked the highest, which were not different from day 42; these days were different ($P \leq 0.05$) from days 3 and 10, and, days 3, 7, and 10 were not different from each other. Considering the KV steers only, the day 10 rectal temperature was lowest across all days, and day 3 was highest and significantly different ($P \leq 0.05$) from days 10, 14, and 28, but not different than day 0, 7, and 42. It is not certain if rectal temperature is solely a response to the BVDV challenge, but the KV and NON steers had increased rectal temperature on days 3 and 7 following challenge whereas MLV steers had lower rectal temperature on these days.

Different strains of BVDV impact their hosts in a variety of ways. Kelling et al. (2002) observed a high response of visual signs of respiratory tract disease and elevated rectal temperature following experimentally induced challenge of 2 highly virulent strains as compared to an equal number of lowly virulent strains. Also, the challenge virus in this project had been previously shown to elevate inoculated cattle's rectal temperatures and project visual signs of morbid behavior without mortality in young Holstein calves (Ridpath et al., 2007).

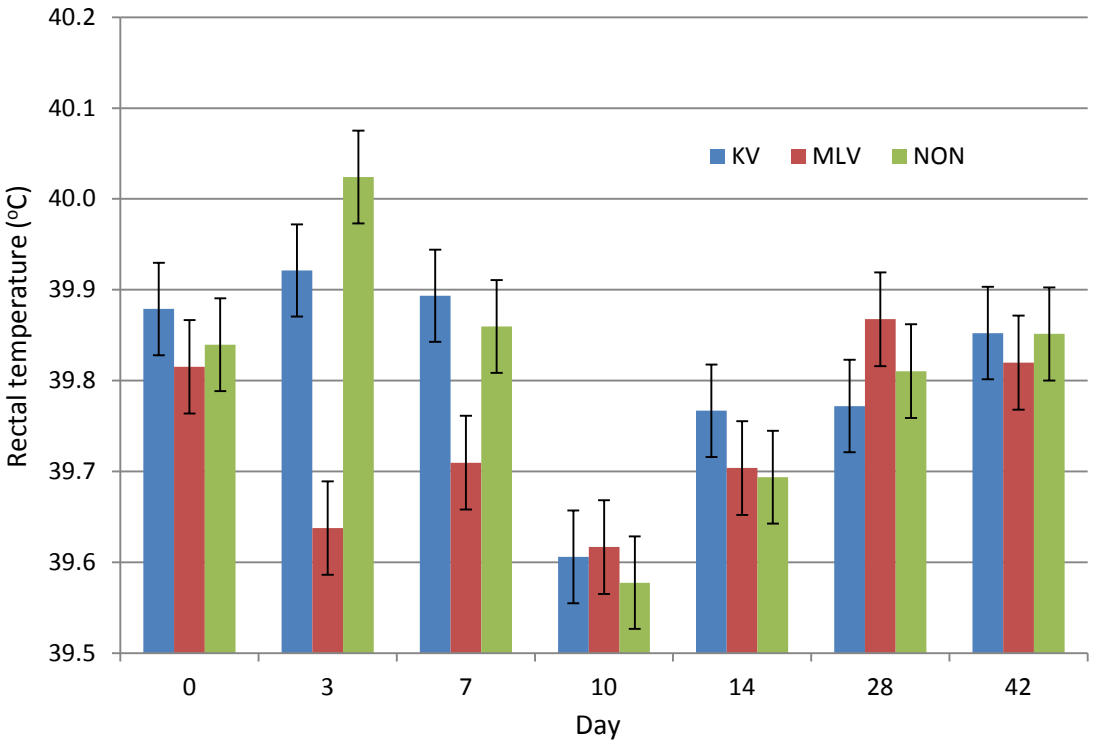

Figure 7. Least squares means of rectal temperature by vaccine type and day. KV = Killed, MLV = modified live, NON = non-vaccinated.

Daily feed intake

Daily feed intake over all days nested within all years is presented in Figure 8. While all 4 years have a similar decreasing pattern through day 7, it appears the 2010, 2011, 2012 daily feed intakes tend to increase through day 23 while 2013 intakes remain lower overall even though the 2013 steers were heavier for weight.

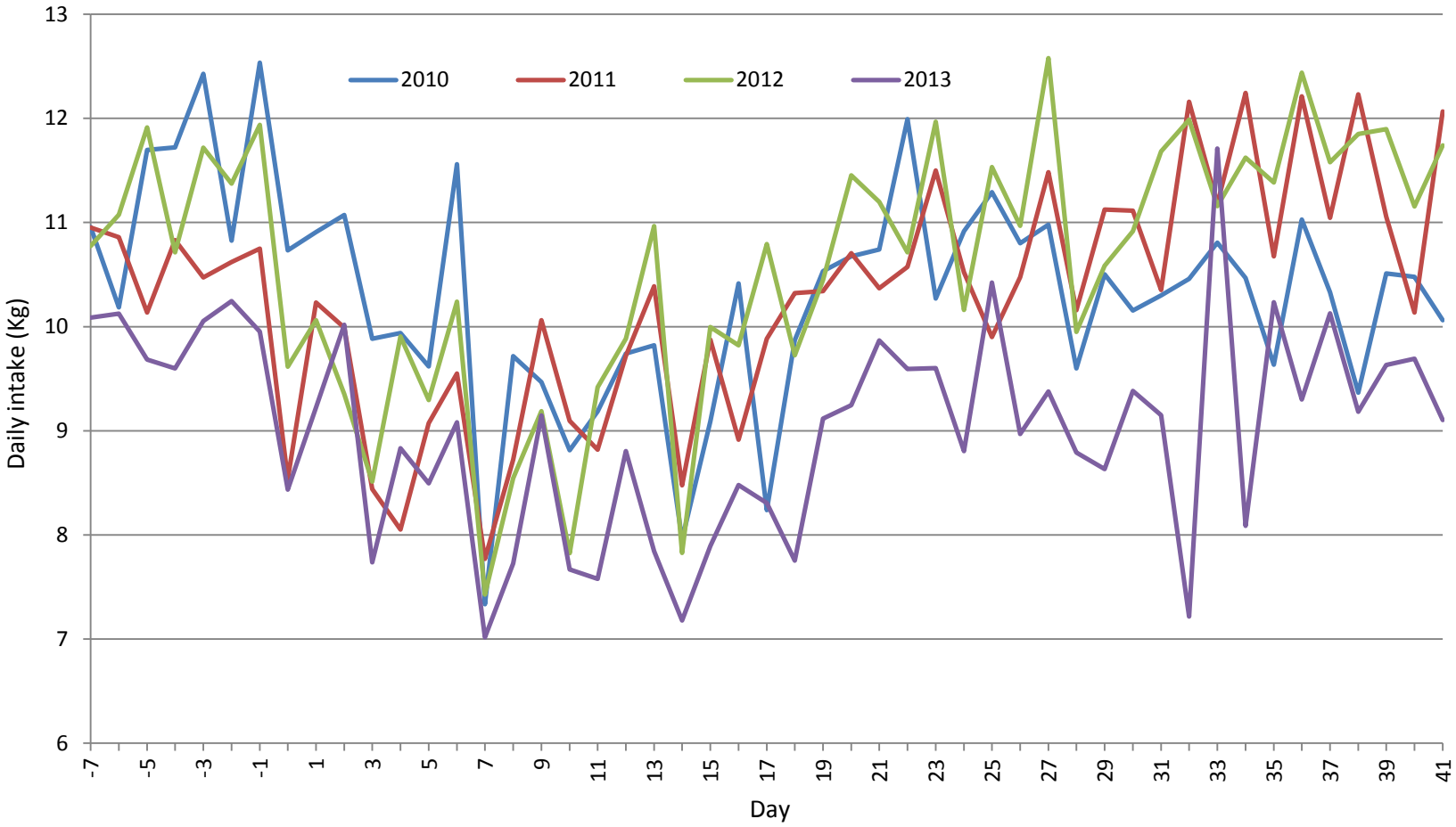

Figure 8. Least squares means of daily feed intake for days within years

Sire was a source of variation for daily feed intake, and these means are given in Figure 9. Steers from sires 494S and 482T had the highest overall least squares means estimates for daily feed intake, and these sires also ranked high for steer weight. While 494S and 482T were not significantly different from each other, 494S was different from the remaining sire groups and 482T was only similar to 539S but significantly higher than the remaining sires as well. Sire groups 230T, 673S, and 8428 were on the lower end of rankings for daily feed intake and were not different from each other; these sires had steers ranked high, low and intermediate, respectively, for progeny weight (shown previously in Figure 2). Steers from sires 673S and 8428 were significantly lower than steers from 14 of the 20 sire groups and 230T being different from 13 of the 20 sire groups.

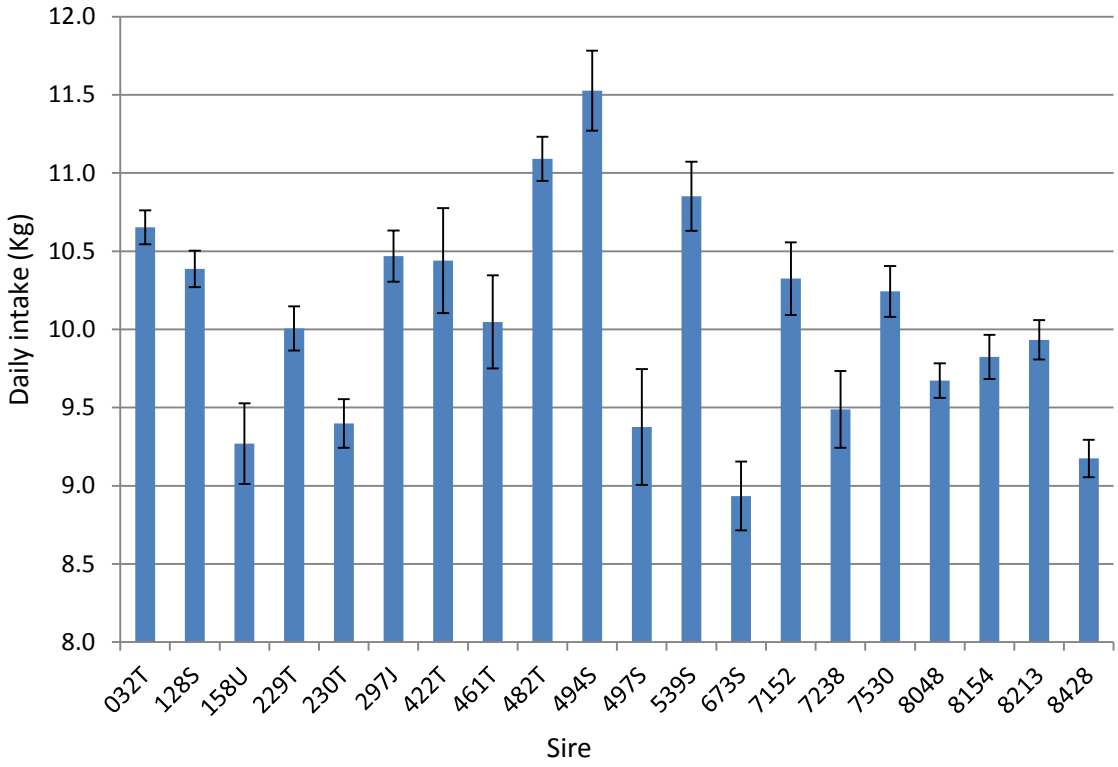

Figure 9. Least squares means of daily feed intake by sire groups

The least squares means for the sire by vaccine type interaction are presented in Figure 10. Sires 494S and 539S ranked among the highest of all sire groups and vaccine type by sire combinations for daily feed intake. The NON steers from sire groups 673S and 7238 ranked among the lowest and were not different from each other. Steers sired by 7238 were significantly different from all sire × vaccine type combinations except 158U-KV, 461T-NON, and 497S-NON whereas 673S was also different ($P \leq 0.05$) from the same sire × vaccine type combinations as 7238-sired calves, with the addition of the MLV steers from within the 673S sire group.

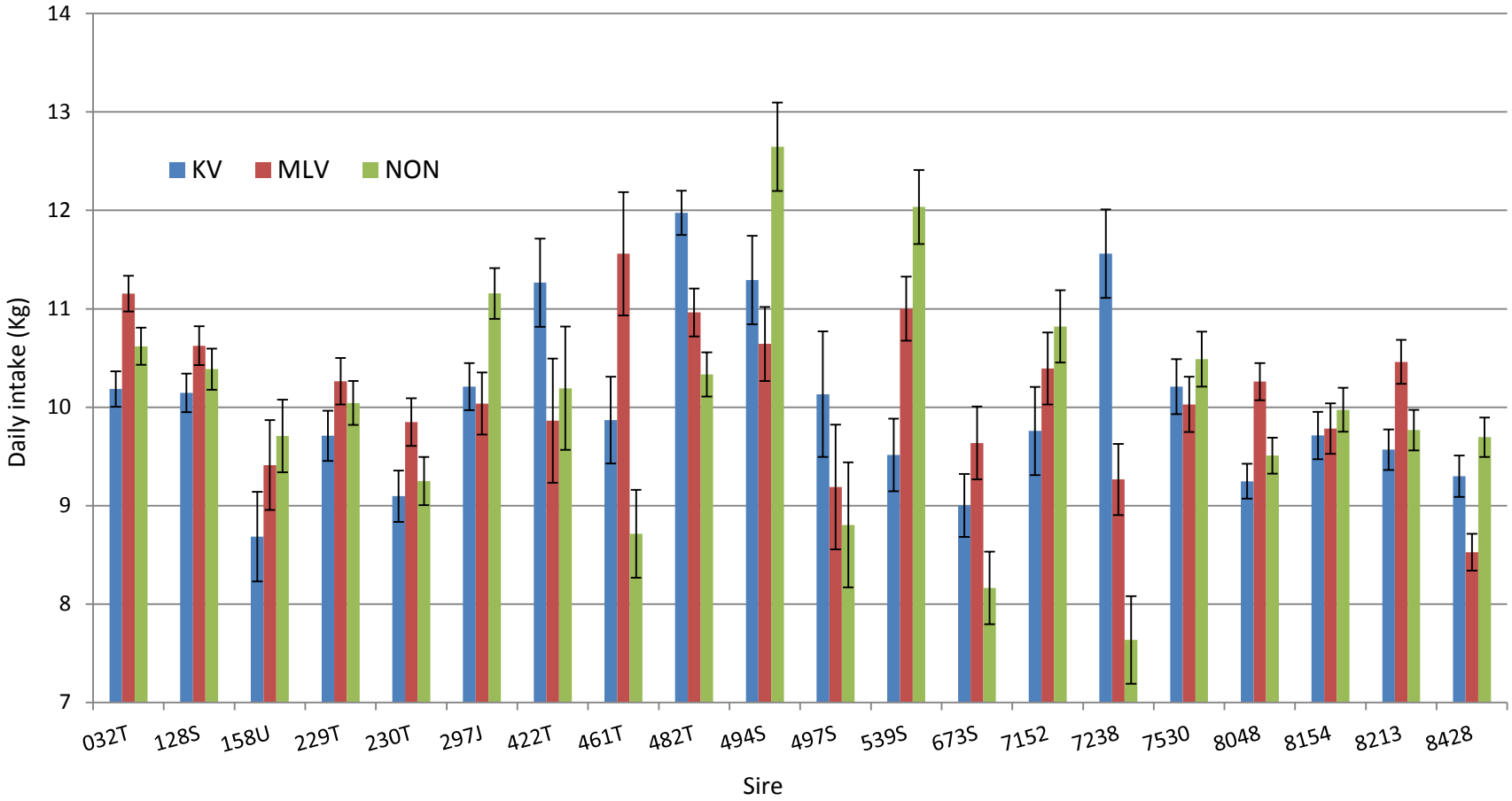

Figure 10. Least squares means of daily feed intake for vaccine type and sire combinations

Variation in the KV vaccine group across sires was not as exaggerated as the NON vaccine group but several differences were still observed. Steers sired by 482T, 494S, 7238, and 422T ranked among the highest for daily feed intake overall of the KV vaccine group and were not different from each other. Steers sired by 482T being the highest least squares means estimate and significantly different from the remaining KV vaccinated steers in other sire groups except the previously mentioned high ranking groups within the KV vaccine type ($P \leq 0.05$). Steers sired by 230T, 7152, 8048, and 8428 were lower ranking for daily feed intake within the KV cattle across sires, were not different from each other and were significantly different from 8 other sire groups, 032T, 128S, 297J, 422T, 482T, 494S, 7238, and 7530 ($P \leq 0.05$).

The least amount of variability across sire groups among the vaccine types was from the MLV group. Steers sire by 461T and 032T were the highest ranking for least squares means for daily feed intake. While progeny by 461T and 032T were not different from each other, sire group 032T was different from 14 of 20 sire groups and not different than 461T, 482T, 494S, 539S, 7152 sired steers, whereas 461T steers were only different from 11 sire groups and not different than 032T, 128S, 422T, 482T, 494S, 539S, 7152, and 8213. The low ranking sire group was 8428 which was different from each other sire group except 158U, 497S, and 7238. As the number of progeny varied across sire groups depending upon their use in breeding, Table 13 provides steer numbers for sires across vaccine group and year of study, and the number of progeny per sire should be considered with these results.

Table 13. Distribution of sires across vaccine groups and years

		Vaccine group			Year			
Sire	Total	KV	MLV	NON	2010	2011	2012	2013
032T	36	13	12	11	0	14	11	11
128S	29	10	10	9	7	0	14	8
158U	7	2	2	3	0	0	0	7
229T	21	6	7	8	0	0	14	7
230T	20	6	7	7	0	20	0	0
297J	17	7	4	6	10	0	7	0
422T	4	2	1	1	0	4	0	0
461T	5	2	1	2	0	2	3	0
482T	23	8	7	8	0	8	0	15
494S	7	2	3	2	0	0	0	7
497S	3	1	1	1	0	0	0	3
539S	10	3	4	3	0	0	0	10
673S	9	4	3	2	0	0	0	9
7152	8	2	3	3	3	3	2	0
7238	7	2	3	2	2	5	0	0
7530	15	5	5	5	3	6	6	0
8048	36	13	11	12	18	9	9	0
8154	21	7	6	8	8	5	8	0
8213	28	10	8	10	5	7	16	0
8428	31	9	12	10	6	15	10	0
Totals[1]	337	114	110	113	62	98	100	77

[1]Relative to steers with known sire and for sires represented across all vaccine groups.

Differences between the vaccine types within a sire group were varied for daily feed intake. In 7 of 20 sire groups there were no differences due to vaccine type. In sire groups 032T, 230T, 461T, 8048, and 8213 the MLV steers had significantly higher feed intake than their NON and KV contemporaries. Two sire groups (482T and 7238) had KV steers with significantly higher intakes, and, two sires (297J and 494S) had NON steers that were the highest for daily feed intake ($P \leq 0.05$). The NON steers were the lowest for feed intake by a significant margin in 4 sire groups (461T, 482T, 673S, and

7238). Only 1 sire group had a KV or MLV vaccine type be the lowest ($P \leq 0.05$) for daily feed intake. In terms of responding to this viral pathogen, the effect of sire × vaccine type was a large contributor to the amount of variation observed for daily feed intake. As defined by the nature of an interaction, the impact of daily feed intake, when comparing vaccine types, depends greatly on the sire group in which those vaccines are used. Overall, it appears that daily feed intake of non-vaccinated steers tended to be more varied as compared to KV and MLV vaccinated cattle, and may indicate increased consistency following pathogen exposure in vaccinated animals. When considering individual sire groups, there was no consistent pattern for daily feed intake between the vaccine types. This implies that the influence of sire groups plays an apparent role in daily feed intake with respect to vaccine strategy. While it does not seem practical to adjust vaccine type for each individual from different sires, these results suggest there is potential to match sire groups with vaccine strategies to maintain suitable daily feed intake levels.

The daily feed intake was also affected by the 3-way interaction of day × vaccine type × high rectal temperature status with these least squares means shown in Figure 11. At day 3 steers classified as NON-YES and KV-YES were lowest for daily feed intake while not being different from each other they were both significantly different from KV-NO, MLV-NO, MLV-YES, NON-NO ($P \leq 0.05$). At day 4 both MLV groups were higher than the KV-NO steers, additionally the MLV-YES steers were different than NON-YES and KV-YES ($P \leq 0.05$). At day 5 all KV and MLV steers were significantly different.

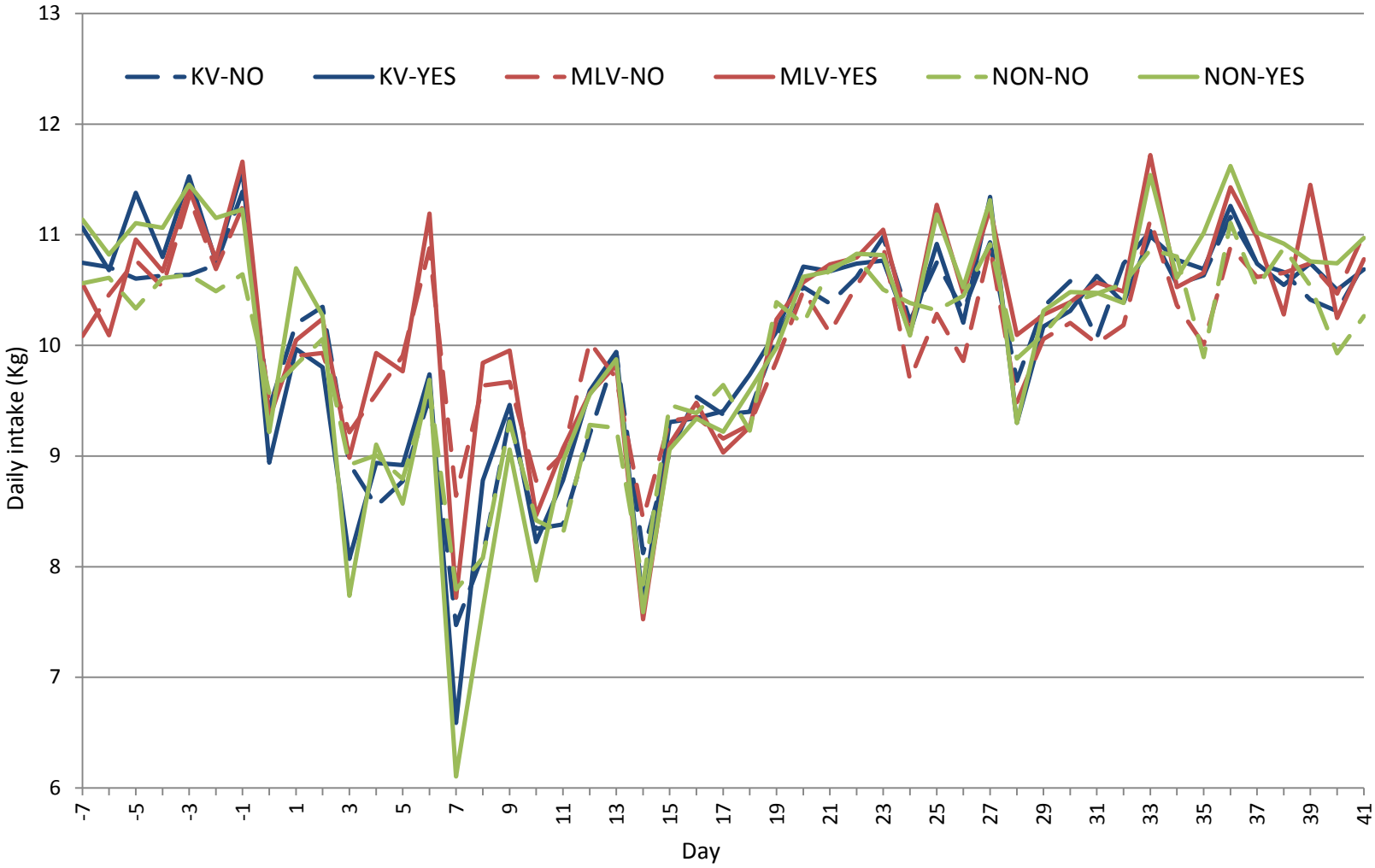

Figure 11. Least squares means of daily feed intake for vaccine type by threshold rectal temperature status. NO = rectal temperature ≤ 40°C; YES = rectal temperature > 40°C for first 14 days following challenge

At day 7, five vaccine type × high temperature combinations were not different but all others were significantly separated. KV-NO was similar to MLV-YES and NON-NO, NON-NO was similar to MLV-YES and MLV-NO, and NON-YES was not different from KV-YES ($P \leq 0.05$). Steers labeled as NON-YES were lowest at day 9 and 10 and only different the MLV-YES and MLV-NO respectively. No differences observed from day 11 through day 13 but at day 14 MLV-NO was different from all steers classified as "YES" regardless of vaccine type but not different from other steers classified as "NO" for rectal temperature status ($P \leq 0.05$).

The overall pattern of daily feed intake tends to decrease sharply from day 0 through day 7, have sharp decreases and increase through day 15 then regain a stable pattern through days 21 and 22. Beyond this, there appears to be a fluctuating nature from 1 day to the next although not as exaggerated as days 7 through 15. Considering the rectal temperature analyses, it seems sensible that increases in rectal temperature status negatively effects daily feed intake, particularly in those cattle of the NON and KV vaccine groups that received antibiotic treatment due to elevated rectal temperature threshold above 40^{o}C.

Daily feed bunk visit frequency

Daily bunk visit frequency was measured to better explain changes in intake and reflect the suppression of appetite or feeding behavior for this trial. Daily bunk visit frequency for all days within all years is presented in Figure 12. In all years the same patterns were observed throughout the 42-day observation period.

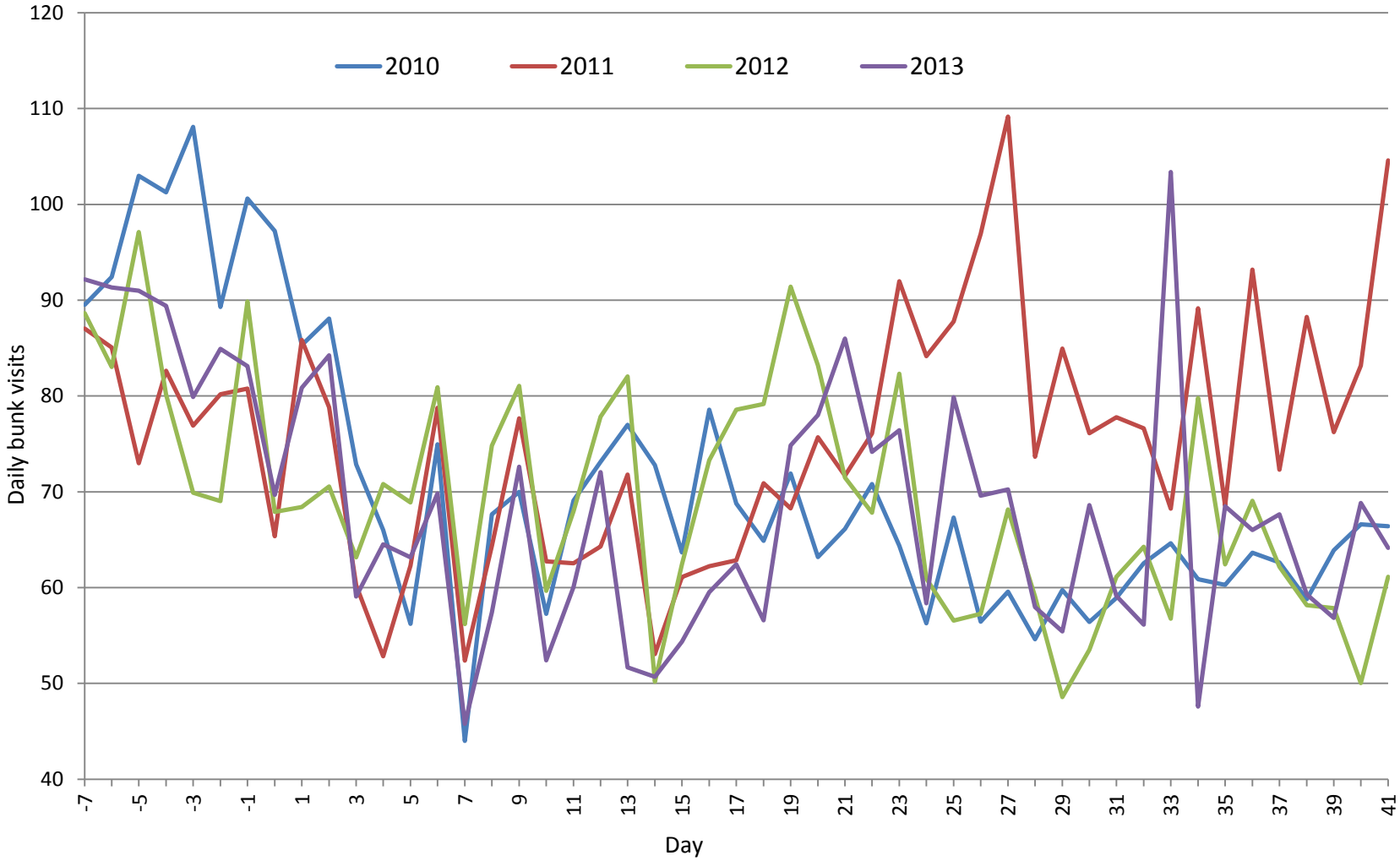

Figure 12. Least squares means of daily bunk visit frequency for days within years

Variation for daily bunk visit frequency was observed for the effect of sire, and the least squares means are found in Figure 13. Progeny from 497S had 9.3 more bunk visits per day than the second highest ranking sire groups which were 461T, 482T, and 8048. While 497S was significantly higher in bunk visits as compared to all other sire groups, 461T, 482T, and 8048 were only different from 11 other sire groups. Sires 461T, 482T, and 8048 were similar to one another, but different ($P \leq 0.05$) from 032T, 128S, 229T, 297J, 494S, 497S, 7152, 7238, 8154, 8213, 8428. There were wide differences in rankings of sires between bunk visits and feed intake. Although 497S was the highest for bunk visits, this sire ranked among the lowest for daily feed intake. Sire 494S ranked the highest for feed intake but was among the lowest for bunk visits. There was no consistent pattern between daily bunk visit and daily feed intake for these sire groups.

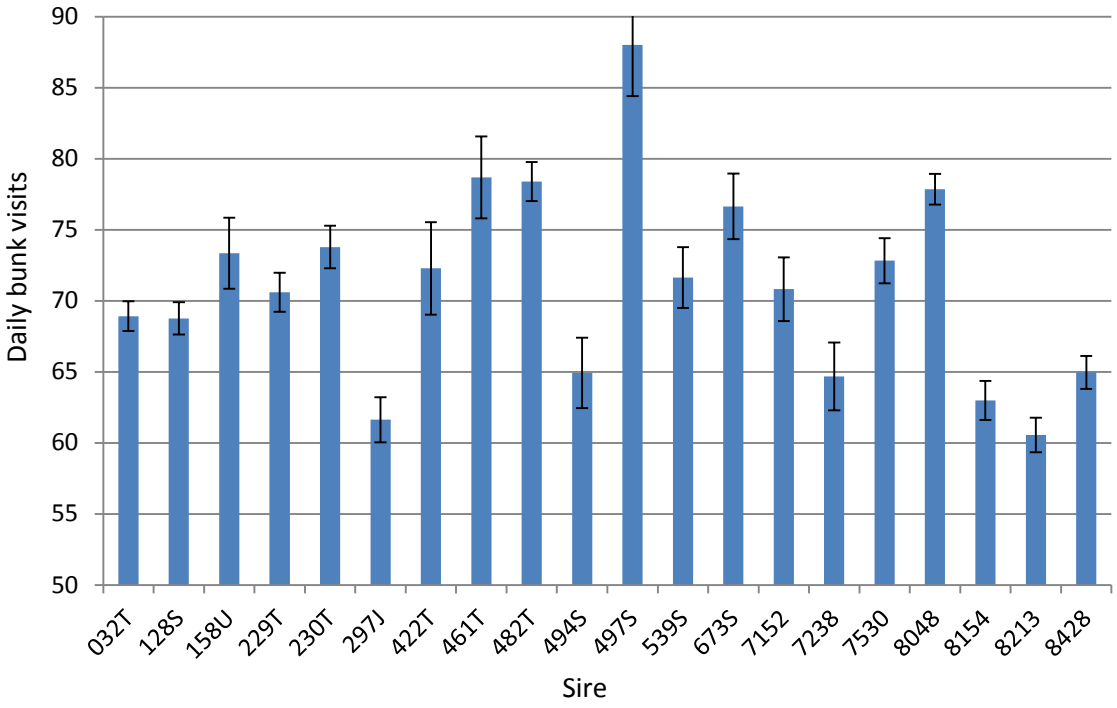

Figure 13. Least squares means of daily bunk visit frequency by sire group

Figure 14 displays the least squares means of daily bunk visit frequency for vaccine type by sire group combinations. When considering the sire × vaccine type interaction, eight sires (229T, 297J, 422T, 673S, 7152, 7530, 8048, and 8154) had no differences for vaccine types among their progeny. Overall, it was observed that 539S-sired steers from the KV vaccine group recorded the lowest bunk visits as compared to his NON and MLV steers, which were not different. Among steers sired by 497S, the MLV group recorded the lowest bunk visits, and the KV and NON steers were not different. The NON steers sired by 7238 were the lowest in his group with MLV steers intermediate and KV highest with all three being different ($P \leq 0.05$). In 6 of the sire groups at least one of the vaccinated groups was higher for bunk visit frequency than

the non-vaccinated steers. When considering attempts to identify patterns, or tendencies with regard sire and vaccine type interaction, there appears to be no constant pattern in terms of bunk visit frequency when considering vaccine type by sire interaction. The lack of identifiable pattern is indicative of substantial genetic differences in an animal's response to viral pathogen exposure with respect to vaccination protocols. As mentioned in the discussion of daily feed intake, under current production systems, it is typically considered impractical to adjust vaccine strategies for each sire's offspring, however, attempts of combining parentage information with preferred vaccine response, has potential of adding to the animals overall well-being by reducing appetite suppression following viral infection.

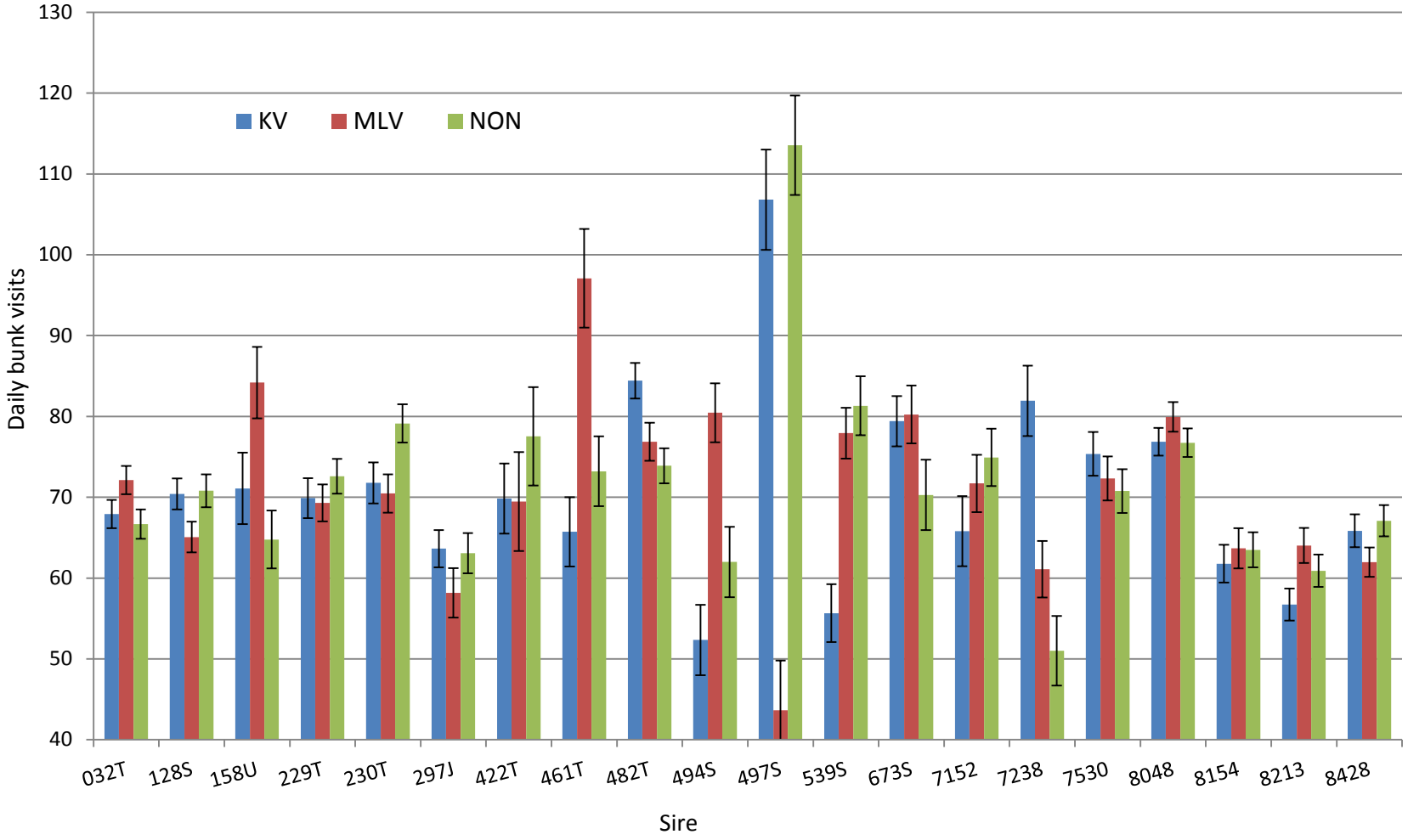

Figure 14. Least squares means of daily bunk visit frequency for vaccine type and sire group combinations.
KV = Killed, MLV = modified live, NON = non-vaccinated

The interaction of vaccine type × day × high rectal temperature was a significant source of variation for daily bunk visit frequency as it was for daily feed intake. The least squares means for daily bunk visits regarding these combinations are shown in Figure 15. In general the pattern of bunk visit frequency is similar to daily feed intake through day 10. Specific differences were observed on days 3 through day 8 where NON-YES steers were constantly lower than both MLV groups, and KV-YES steers on days 4 and 8. At days 4 through 8 the MLV steers had more bunk visits regardless of rectal temperature status than the NON-YES steers, additionally all MLV-YES steers were consistently higher than all KV steers at days 4 to 6. From days 9 to 13 no differences were observed between any vaccine type × rectal temp status combination but at day 14 through 17 the NON-YES frequented the feed bunk the least amount and the NON-NO frequented the feed bunk the most, with these classifications being different ($P \leq 0.05$) from each other. Buhman et al. (2000) observed some similar patterns in that newly arrived feedlot cattle that were classified as morbid had lower frequency and duration days 11 through 27. Additionally Sowell et al. (1999) observed healthy cattle from visual assessments had more bunk visits each day, and had longer duration time at those bunk visits.

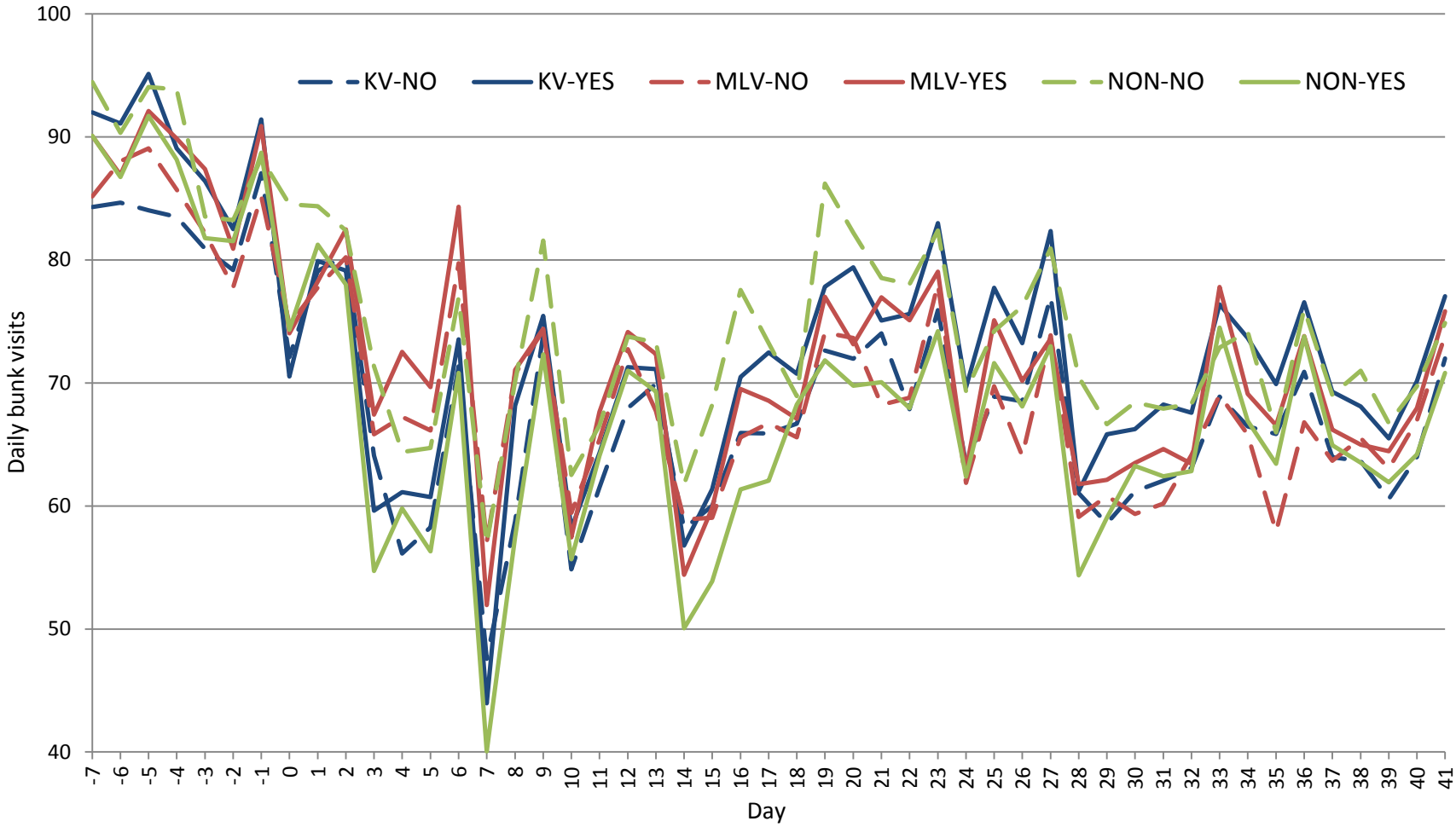

Figure 15. Least squares means of daily bunk visit frequency for vaccine type and rectal temperature status combinations. KV = Killed, MLV = modified live, NON = non-vaccinated, NO = rectal temperature ≤ 40°C; YES = rectal temperature > 40°C during 14 days post challenge.

Average daily gain

Steers exceeding the rectal temperature threshold of 40^{o}C on d 1 though 14 exhibited a 0.24 kg/d reduction (P = 0.02) in ADG the first 14-d period following viral challenge, then gained 0.18 kg/d more (P = 0.02) during the final 14-d period as compared to steers that did not exceed the 40^{o}C threshold (Figure 16). Although there was no significant difference for steers above or below the 40^{o}C threshold in the second 14-d period, both groups exhibited an increase in ADG during this period compared to the first 14-d period and last 14-d period. These results from d 0 to 14 are similar to Roeber et al. (2001) who observed a 0.25 kg/d reduction in ADG in newly received preconditioned cattle identified as morbid and Schneider et al. (2009) who reported 0.07 kg/d ADG reduction in cattle throughout the feeding phase for cattle receiving BRD treatment. Results from days 14 to 28 in this trial also agree with data presented by Wittum et al. (1996) who observed no differences in ADG for treated cattle as compared to non-treated cattle. The data from the first 14-d period also tends to agree with Gardner et al. (1999) in that a 0.06 kg/d reduction in ADG was observed for cattle with a rectal temperature great than 40^{o}C and having visual BRD symptoms. Results from these data suggests that cattle expressing high rectal temperatures experience reduced growth performance while cattle not expressing high temperatures are affected less severely 0 to 14 days following viral exposure. All cattle compensated ADG days 14 to 28, and steers with rectal temperatures above 40^{o}C in the first- 14 days had higher ADG 28 to 42 days following viral challenge with this BVDV strain.

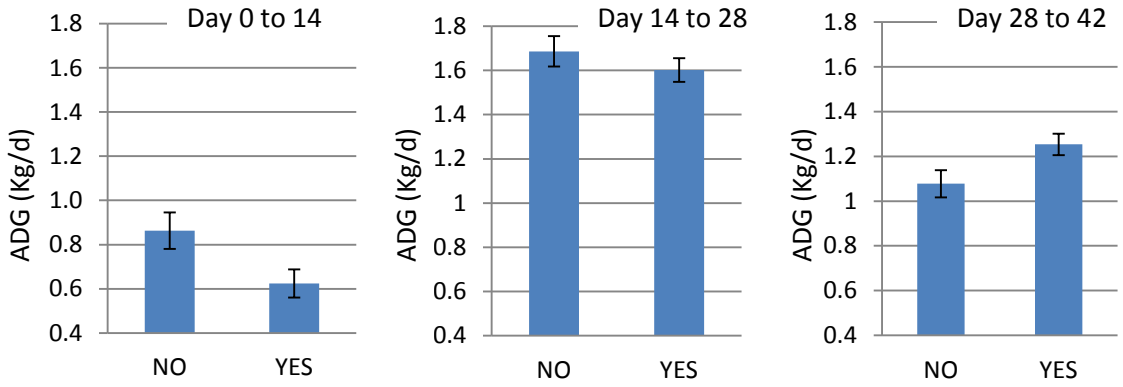

Figure 16. Average daily gain for steers that did not (NO) versus did (YES) exceed rectal temperature threshold of 40.0°C in days 0 to 14 (left), days 14 to 28 (center), and days 28 to 42 (right).

With the strain of BVDV evaluated in this study, overall ADG was not different between steers that had elevated rectal temperature even though differences within periods existed, and the rectal temperature status interacted with vaccine type (Figure 17). Considering the vaccine type × high temperature status combination, the non-vaccinated steers exhibited the highest and lowest values for ADG for days 14 to 28. The non-vaccinated steers that did not have a high rectal temperature (NON-NO) were significantly higher for ADG as compared to KV-NO, MLV-NO, and NON-YES steers. Conversely, non-vaccinated steers that exceeded rectal temperature threshold (NON-YES), were significantly lower for ADG as compared to NON-NO, MLV-YES, and KV-YES steers. Steers in the KV vaccine group were not different from steers in the MLV group. It seems that NON steers classified as morbid by elevated rectal temperature were at increased risk for reduction of ADG. Even though the NON vaccinated steers who did

not exhibit high rectal temperatures have increased ADG days 14 through 28 following challenge, it may not compensate for the higher proportion of NON vaccinated steers that have reduced ADG.

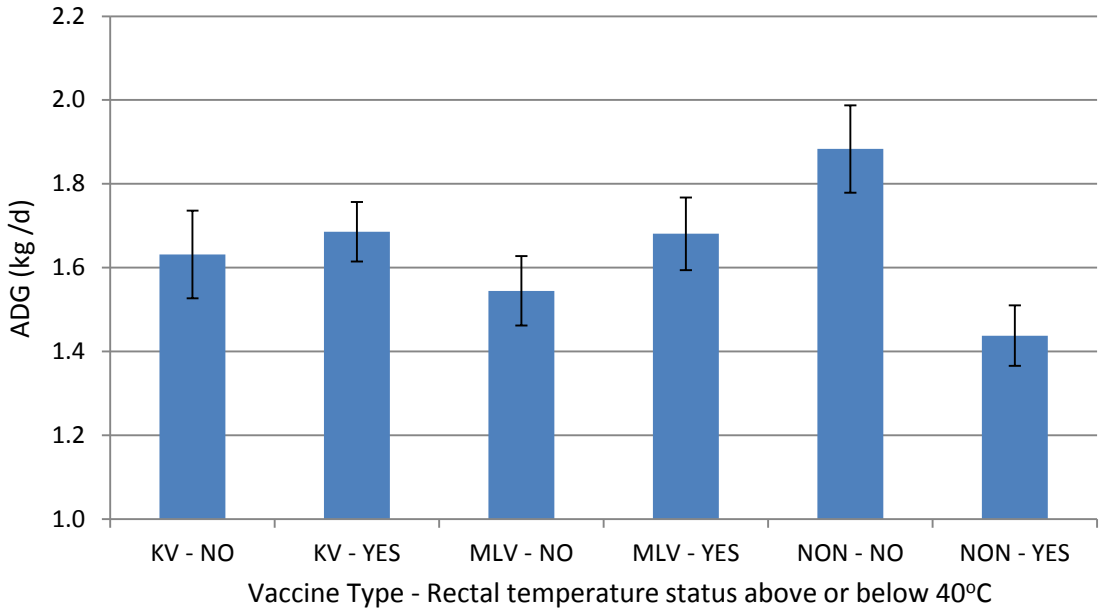

Figure 17. Least squares means for ADG from days 14 to 28 across vaccine type and rectal temperature status. KV = Killed, MLV = modified live, NON = non-vaccinated, NO = rectal temperature ≤ 40° C; YES = rectal temperature > 40° C.

The least squares means presented in Figure 18 represent the variation for sire group as a source of variation for ADG during the second 14 day period, (days 14 to 28). Steers sired by 497S were the highest followed by 7530 and 8154 and these sire groups were only different than 6 or few other sire groups respectively and not different from each other. Overall it was observed that 9 sire groups were not different from any other sire group. The influence of sire alone reflects genetic influence for growth due

to sire and is therefore important to consider when investigating the impacts of health associated measures on growth and production traits.

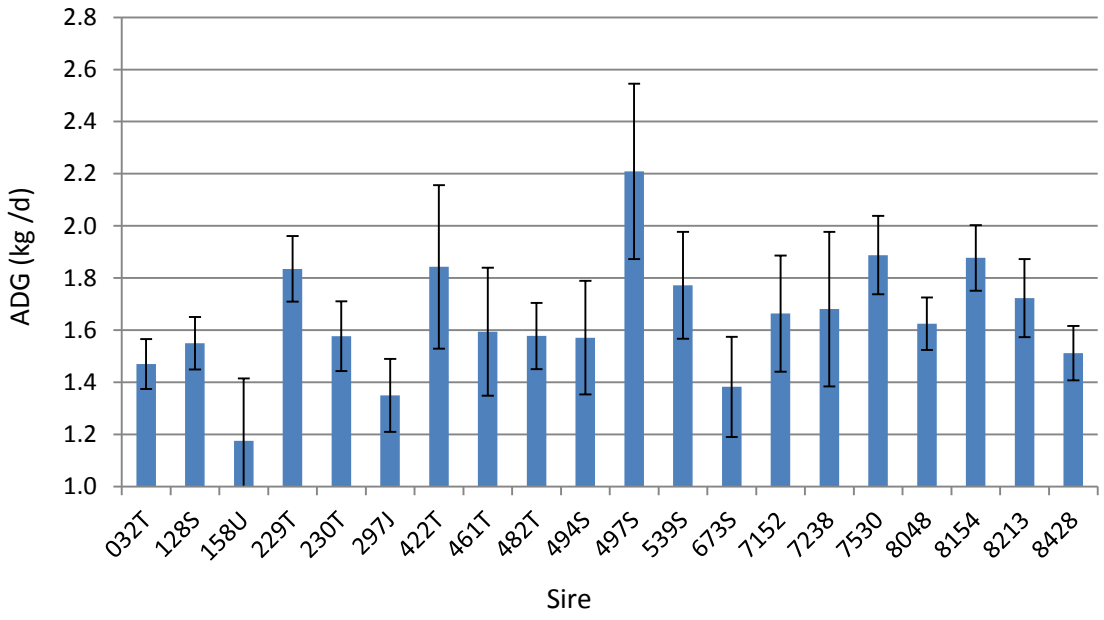

Figure 18. Least squares means for ADG from days 14 to 28 by sire groups

Morbidity and lung scores

Visual clinical symptoms were recorded twice daily on days 0 to 14, and the distribution of those clinical scores are displayed in Table 14. In general, very few visual symptoms of morbidity were observed in any year, and animals that were documented with any signs were almost exclusively scored a 1. No steers received other than a 0 for diarrhea, and, signs of depression, coughing and gauntness were the main morbidity conditions noticed. Chi-square tests were conducted to test the relationship of the distributions but overall no significant differences were detected for visual clinical signs across other study factors.

Table 14. Distributions of clinical sign category during the 14-day period following challenge across other study factors

	Year of trial			
Category[1]	2010	2011	2012	2013
No	64 (82.1%)	91 (87.5%)	87 (82.9%)	85 (91.4%)
Yes	14 (17.9%)	13 (12.5%)	18 (17.1%)	8 (8.6%)
Total	78	104	105	93

	Vaccine type		
	Killed	Modified live	Non-vaccinated
No	112 (88.2%)	113 (89.0%)	102 (80.9%)
Yes	15 (11.8%)	14 (11.0%)	24 (19.1%)
Total	127	127	126

	Feedlot pen			
	1	2	3	4
No	81 (85.3%)	87 (90.6%)	82 (86.3%)	77 (81.9%)
Yes	14 (14.7%)	9 (9.4%)	13 (13.7%)	17 (18.1%)
Total	95	96	95	94

[1]No = no sign of morbidity, Yes = any sign of morbidity. Animals were evaluated twice per day by the same evaluator across all years. Only minor signs (1 or 2 on a 1-to-5 scale) of depression, coughing or gauntness were documented.

The lung score data are summarized in Table 15. From the three years 2010 to 2012, 60.8% of cattle exhibited high rectal temperature status and received therapeutic antibiotic treatment. Of the cattle that showed rectal temperature over 40.0 C, 22.4% had no lung tissue discoloration (score of 1), 55.8% displayed the lowest level of discoloration (score of 2), and 21.8% had lung scores of 3 or greater, indicating evidence that lung tissue disruption was visually evident on more than 25% but less than 75% of the lung.

The 22.4% of the steers that were treated for elevated rectal temperature but had no evidence of lung discoloration is similar to results of Wittum et al. (1996) who observed 22.0%. Bryant et al. (1999), Gardner et al. (1999), and Schneider et al. (2009) observed higher percentages of treated cattle with no lung color disruption at 63.0%, 37.0%, and 36.0%, respectively. The potentially more concerning perspective from a production management, animal well-being and clear understanding of BRD is analyses of cattle that did not exhibit a high rectal temperature but still displayed evidence of lung discoloration.

Table 15. Distribution of lung color scores across other study factors

	Year of trial		
Lung score	2010	2011	2012
1	20 (25.6%)	32 (31.1%)	24 (22.9%)
2	41 (52.6%)	55 (53.4%)	55 (52.4%)
3	16 (20.5%)	16 (15.5%)	23 (21.9%)
4	1 (1.3%)	0	3 (2.8%)
Total	78	103	105

	Vaccine type		
	Killed	Modified-live	Non-vaccinated
1	23 (24%)	25 (26.6%)	28 (29.2%)
2	49 (51%)	49 (52.1%)	53 (55.2%)
3	22 (22.9%)	19 (20.2%)	14 (14.6%)
4	2 (2.1%)	1 (1.1%)	1 (1%)
Total	96	94	96

	Feedlot pen			
	1	2	3	4
1	21 (29.6%)	16 (22.5%)	17 (23.9%)	22 (30.1%)
2	35 (49.3%)	41 (57.8%)	38 (52.5%)	37 (50.7%)
3	14 (19.7%)	12 (16.9%)	16 (22.6%)	13 (17.8%)
4	1 (1.4%)	2 (2.8%)	0	1 (1.4%)
Total	71	71	71	73

	Evidence of visual signs	
	No	Yes
1	66 (27.4%)	10 (22.2%)
2	122 (50.6%)	29 (64.5%)
3	49 (20.3%)	6 (13.3%)
4	4 (1.7%)	0
Total	241	45

	Rectal temperature threshold	
	Below	Above
1	37 (33%)	39 (22.4%)
2	54 (48.2%)	97 (55.8%)
3	21 (18.8%)	34 (19.5%)
4	0	4 (2.3%)
Total	112	174

Only 33% of the cattle below 40^{o}C threshold had lung color score of 1 which indicated ideal lung color, with no visual discoloration or evidence of infection; 48.2% of the cattle with below 40^{o}C had a lung score of 2, and 18.8% had a score of 3 (discoloration of greater than 25% but less than 50% of the visual lung tissue). As compared to prior studies, these numbers are within the similar ranges of observations made Bryant et al. (1999), Buhman et al. (2000), Gardner et al. (1999), Schneider et al. (2009), Thompson et al. (2006), and Wittum et al. (1996) which reported 42.0%, 83.3%, 29.0%, 60.6%, 38.4%, and 68.0%, respectively for cattle with lung lesions present but were not treated due to BRD morbidity.

These observations illustrate the importance of the incidence of sub-clinical illness in beef cattle feeding systems and reinforce the lack of accurate detection methods currently in place. Considering the visual signs of morbidity alone, no therapeutic treatments would have been administered in this trial. This differs in comparison with the afore mentioned trials with lung lesion data, as at least part of the pulling and treating criteria involved visual signs of illness of pen riders or research personnel in those studies. This element of human variation between studies also highlights the subjective nature of clinical evaluation and the profound need for development of effective methods of early and accurate BRD diagnosis.

SUMMARY

The long-term goal leading to generation of steers for this project was development of a cattle population useful for genomic investigations of numerous economically important traits, with Nellore and Angus foundation animals and resulting crosses utilized. Subsequently, the objective for this dissertation was to characterize phenotypes associated with production measures of feed intake, feeding frequency, growth performance, and morbidity aspects of these *Bos indicus-Bos taurus* crossbred steers of known genetic background following BRD vaccination and BVDV challenge that could eventually be used for genetic mapping and related genomic studies. Combining major areas of influence such as growth, immune response, and information of genetic backgrounds is relevant and is likely needed to better explain the relationships among these areas and how they collectively affect the overall well-being of cattle in beef production systems. In an attempt to study some of these relationships, this project evaluated weight, rectal temperature, visual signs, feed intake, feed bunk visit frequency and weight gain in steers where the genetic background, vaccination protocol, and pathogen challenge were known. All cattle were verified to be free of BVDV persistent infection before the trial began.

Weight was significantly influenced by day within year, year, sire, with a trend for a day × vaccine type interaction ($P = 0.09$), and the vaccine type by day approached significance as KV steers tended to be lighter across all days. Since steers were

stratified so that sires were represented across all vaccine types, there was no sire × vaccine type interaction on weight. None of these results were particularly surprising.

Rectal temperature was significantly influenced by day within year, year, and sire as was weight; however, pen within year, vaccine type and day by vaccine type interaction influenced rectal temperature only. Across vaccine types, the MLV steers were lower than KV and NON steers; this corresponded with a lower proportion of MLV steers being identified above the 40^{o}C rectal temperature threshold established for antibiotic treatment. Steers from the MLV group had lower rectal temperature than KV and NON steers at days 3 and 7 implying that this group may have been less impacted by the BVDV challenge.

In general daily feed intake and daily bunk visit frequency decreased from day 0 through day 7 and increase gradually after that in all years, and this is interpreted as being the result of the BVDV challenge. However, the patterns in both these traits were not the same across sire × vaccine type combinations or across day × vaccine type × rectal temperature status combinations. For daily feed intake, variation from the sire group × vaccine type interaction was observed where steers in the NON group ranked lowest in 4 sire groups. Much less variation between sires for daily feed intake was observed for both vaccinated groups, which can be a production advantage when vaccination is utilized; no consistent pattern was identified between all three vaccine types suggesting the potential of matching genotypes and vaccine strategies for

optimum feed intake levels considerations, or that inherent variability may remain when all animals are vaccinated the same and exposed to the same pathogen.

While both daily feed intake and daily bunk visit frequency were significantly influenced by the same effects statistically, the relationship of these variables is subject to interpretation due to the fact that sire groups and vaccine type by sire group combinations were not similar in many cases between these two traits; an increase in daily bunk visit did not translate into higher daily feed intake. Instead, some sire groups were exactly opposite of this, indicating changes in appetite in response to viral exposure and vaccine effectiveness can alter aggressiveness of appetite, ultimately altering feeding behavior, and that this relationship can be varied across family lines.

Rectal temperature status above the 40^{o}C threshold contributed to reduced ADG in days 0 through 14 and again for days 28 through 42, but not for days 14 to 28 or overall from days 0 to 42. The vaccine type by threshold rectal temperature status interaction also was an important source of variation for ADG in that non-vaccinated steers below the 40^{o}C threshold were the highest for ADG at days 14 to 28 (possibly when they are recovering from viral infection), but the non-vaccinated steers over the 40^{o}C threshold were significantly lower for ADG during this period. Visual signs of illness for this project were not distributed differently among other study factors, which was also the case for lung color scores although 67% of cattle below 40^{o}C threshold exhibited some amount of visual discoloration. This reinforces the need for enhanced

BRD detection methods as opposed to visual evaluation or rectal temperature status alone.

These data display evidence of variation of measured values that would relate to vaccine response following virus exposure and further impacts on feeding behavior and intake. Observations from this project promote further discussion of the influence that genetics have on BVDV (and other pathogen) infection and effectiveness of genetic interactions with vaccine protocols. Considering the number of strains of BVDV and the varying levels of virulence that are associated among those strains, it is not unreasonable to speculate about the true prevalence and potential subclinical influences of BVDV in various production settings. Future research could expound on differences in breeds, impact due to degree of heterozygosity from crossbreeding, differences due to the percentage of *Bos indicus* influence, or even maternal breed type and paternal breed type reciprocals. The degree of variation within and across sire groups in these data suggests that identification of genomic influences has strong potential. Additional measures of health status beyond rectal temperature and visual clinical symptoms such as immune systems cellular functions need further investigation as well, to help quantify the response variables associated with viral pathogen exposure.

LITERATURE CITED

Abbas, A. K. and A. H. Lichtman. 2007. Cellular and Molecular Immunology. Elsevier Saunders ed. Philadelphia, PA. 4-6.

Ahn, B.C., P.H. Walz, G.A. Kennedy, S. Kapil. 2005. Biotype, genotype, and clinical presentation associated with bovine viral diarrhea virus (BVDV) isolates from cattle. Intern. J. Appl. Res. Vet. Med. 3:319-325

Baker, J.C. 1995. The clinical manifestations of bovine viral diarrhea infection. Vet Clin North Am Food Anim Pract. 11:425-445.

Baker, J., C. York., J. Gillepsie, and G. Mitchell. 1954. Virus diarrhea in cattle. Am. J. Vet. Res. 15:525-531.

Blecha, F., S. L. Boyles, and J. G. Riley. 1984. Shipping suppresses lymphocyte blastogenic responses in Angus and Brahman × Angus feeder calves. J. Anim. Sci. 59:576-583.

Booker, C. W. S. M. Abutarbush, P. S. Morley, G. K. Jim, T. P. Pittman, O. C. Schunicht, T. Perret, B. K. Wildman, R. K. Fenton, P. T. Guichon, and E. D. Janzen. 2008. Microbiological and histopathological findings in cases of fatal bovine respiratory disease of feedlot cattle in western Canada. Can. Vet. J. 49:473-481.

Bryant, L K., L. J. Perino, D. Griffin, A. R. Doster, and T. E. Wittum. 1999. A method for recording pulmonary lesions of beef calves at slaughter and the association of lesions with average daily gain. Bovine Pract. 33:163-173.

Buhman, M.J., L.J. Perino, M.L. Gaylean, T.E. Wittum, T.H. Montgomery, and R.S. Swingle. 2000. Association between changes in eating and drinking behaviors and respiratory tract disease in newly arrived calves at a feedlot. Am. J. Vet. Res. 61:1163-1168.

Callan, R. J., and F. B. Garry. 2002. Biosecurity and bovine respiratory disease. Vet. Clin. North. Am. Food. Anim. Pract. 18:57-77.

Chase, C.L., D.J. Hurley, and A.J. Reber. 2008. Neonatal immune development in the calf and its impact on vaccine response. Vet Clin Food Anim. 24:87-104.

Chirase, N.K., and L.W. Greene. 2001. Dietary zinc and manganese sources administered from the fetal stage onwards affect immune response of transit stressed and virus infected offspring steer calves. Anim. Feed Sci. and Tech. 93:217-228.

Cornish, T.E., A.L. van Olphen, J.L. Cavendar, J.M. Edwards, P.T. Jaeger, L.L. Vieyra, L.F. Woodward, D.R. Miller, D. O'Toole. 2005. Comparison of ear notch immunohistochemistry, ear notch antigen-capture ELISA, and buffy coat virus isolation for detection of calves persistently infected with bovine viral diarrhea virus. J. Vet. Diagn. Invest. 17:110-117.

Cortese, V. S., R. Whittaker, and J. Ellis. 1998. Specificity and duration of neutralizing antibodies induced in healthy cattle after administration of a modified-live virus vaccine against bovine viral diarrhea. Am. J. Vet. Res. 59:848-850.

Cravey, M. 1996. Preconditioning effect on feedlot performance. In: Proc. Southwest Nutrition and Management Conference. Feb. 26, Phoenix, AZ pp33-37.

Daniels, T.K., J.G.P. Bowman, B.F. Sowell, M.E. Branine, and M.E. Hubbert. 2000. Effects of metaphylactic antibiotics on behavior of feedlot calves. Professional Animal Scientist. 16:247-253.

Duff, G. C., and M. L. Galyean. 2007. Board-Invited Review: Recent advances in management of highly stressed, newly received feedlot cattle. J. Anim. Sci. 85:823-840.

Edwards, A.J. 1996. Respiratory diseases of feedlot cattle in the central USA. Bovine Pract. 30:5-7.

Edwards, S., L. Wood, C. Hewitt-Taylor, and T.W. Drew. 1986. Evidence for an immunocompromising effect of bovine pestivirus on bovid herpesvirus-1 vaccination. Vet. Res. Commun. 10:297-302.

Edwards, T.A. 2010. Control methods for Bovine Respiratory disease for Feedlot Cattle. Vet Clin Food Anim. 26:273-284.

Faries, F. C. Jr. 1999. Cattle Vaccines. bull. pub. No. L-5289. Texas Ag. Ext. Service. Texas A&M University, College Station, TX.

Frank, G. H., R. E. Briggs, G. C. Duff, and H. S. Hurd. 2003. Effect of intranasal exposure to eukotoxin-deficient *Mannheimia haemolytica* at the time of arrival at the feedyard on subsequent isolation of *M. haemolytica* from nasal secretions of calves. Am. J. Vet. Res. 64:580-585.

Fulton, R. W., A. W. W. Confer, and L. J. Burge. 1995. Antibody responses by cattle after vaccination with commercial viral vaccines containing bovine herpesvirus-1, bovine viral diarrhea virus, parainfluenza-3 virus, and bovine respiratory syncytial virus immunogens and subsequent revaccination at day 140. Vaccine. 13:725-733.

Fulton, R. W., and L. J. Burge. 2000a. Bovine viral diarrhea virus types 1 and 2 antibody response in calves receiving modified live virus or inactivated vaccines. Vaccine. 19:267-274.

Fulton, R.W., B. Hessman, B.J. Johnson, J.F. Ridpath, J.T.Saliki, L.J. Burge, D. Sjeklocha, A.W. Confer, R.A. Funk, and M.E. Payton. 2006. Evaluation of diagnostic tests used for detection of bovine viral diarrhea virus and prevalence of subtypes 1a, 1b, and 2a in persistently infected cattle entering a feedlot. J. Am. Vet. Med. Assoc. 228:578-584.

Fulton, R.W., C.W. Purdy, A.W. Confer, J.T. Saliki, R.W. Loan, R.E. Briggs, L.J. Burge. 2000b. Bovine viral diarrhea viral infections in feeder calves with respiratory disease: Interactions with pasteurella spp., parainfluenza-3 virus, and bovine respiratory syncytial virus. Can. J. Vet. Res. 64:151-159

Fulton, R.W., J.F. Ridpath, A.W. Confer, J.T. Saliki, L.J. Burge, and M.E. Payton. 2003b. Bovine viral diarrhea virus antigenic diversity: impact on disease and vaccination programmes. Biologicals. 31:89-95.

Fulton, R.W., J.F. Ridpath, B. Hessman, and K.S. Blood. 2009. Bovine viral iarrhea virus variability and prevalence of BVDV subtypes in persistently infected cattle entering feedlots: BVDV1b as predominant subtype. Proc. 4th U.S. BVDV Symposium, Jan. 25-27, Phoenix, AZ (session 1).

Fulton, R.W., J.F. Ridpath, J.T. Saliki, R.E. Briggs, A.W. Confer, L.J. Burge, C.W. Purdy, R.W. Loan, F.C. Duff, and M.E. Payton. 2002. Bovine viral diarrhea virus (BVDV) 1b: predominant BVDV subtype in calves with respiratory disease. Can. J. Vet. Res. 66:181-190.

Fulton R. W., J. T. Saliki, L. J. Burge, and M. E. Payton. 2003a. Humoral immune response and assessment of vaccine virus shedding in calves receiving modified live virus vaccines containing bovine herpesvirus-1 and bovine viral diarrhea virus 1a. J. Vet. Med B 50:31.

Fulton, R.W., R.E. Briggs, J.F. Ridpath, J.T. Saliki, A.W. Confer, M.E. Payton, G.D. Duff, D.L. Step, and D.A. Walker. 2005. Transmission of bovine viral diarrhea virus 1b to

susceptible and vaccinated calves by exposure to persisitently infectd calves. Can. J. Vet. Res. 69:161-169.

Galyean, ML., L. J. Perino, and G. C. Duff. 1999. Interaction of cattle health / immunity and nutrition. J. Anim. Sci. 77:1120-1134.

Gardner, B. A., H. G. Dolezal, L. K. Bryant, F. N. Owens, and R. A. Smith. 1999. Health of finishing steers: Effects on performance, carcass traits, and meat tenderness. J. Anim. Sci. 77:3168-3175. Griffin, D. 1997. Economic impact associated with respiratory disease in beef cattle. Vet. Clinics of N. Am. Food Anim. Pract. 13:367-377.

Hessman, B. E., R. W. Fulton, D. B. Sjeklocha, T. A. Murphy, J. F. Ridpath, and M. E. Payton. 2009. Evaluation of economic effects and the health and performance of the general cattle population after exposure to cattle persistently infected with bovine viral diarrhea virus in a starter feedlot. Am. J. Vet. Res. 70:73-85.

Hutcheson, D. P. and N. A. Cole. 1986. Management of transit-stress syndrome in cattle: Nutritional and environmental effects. J. Anim. Sci. 62:555-560.

Kelling, C.L., D.J. Steffen, C.L. Topliff, K.M. Eskridge, R.O. Donis, D.S. Higuchi. 2002. Comparative virulence of isolates of bovine viral diarrhea virus type II in experimentally inoculated six to nine month old calves. Am. J. Vet. Res. 63:1379-1384.

Lalman, D, S. Hutson, W. Shearhart, C. Ward, and S. McKinley. 2005. Preconditioning reduces sickness and death loss in weaned calves. J. Anim. Sci. 83(Suppl. 2):21.

Larson, R.L., V.L. Pierce, and D.M. Grotelueshen, and T.E. Wittum. 2002. Why Control BVD: Economic and production costs, tools to accomplish. Available: http://www.ars.usda.gov/SP2UserFiles/Place/36253000/BVD2005/Produce1_Larson_Hout.pdf. Accessed June 10, 2008.

Liebler-Tenorio, E.M. J.F. Ridpath, J.D. Neill. 2003. Lesions and tissue distribution of viral antigen in severe acute versus subclinical acute infection with BVDV2. Biologicals. 31:119-122.

Loneragan, G. H., D. U. Thomson, D. L. Montgomery, G. L. Mason, and R. L. Larson. 2005. Prevalence, outcome, and health consequences associated with persistent infection with bovine viral diarrhea virus in feedlot cattle. J. Am. Vet. Med. Assoc. 226:595-601.

Martin, S.W., A.H. Meek, D.G. Davis, J.A. Johnson, and R.A. Curtis. 1982. Factors associated with mortality and treatment costs in feedlot calves: The Bruce County beef project, years 1978, 1979, 1980. Can. J. Comp. Med. 46:341-349.

Mathis, C.P. 2008. Preconditioning programs: Approaches, economics, and subsequent performance. Proc. Plains Nutrition Council Spring Conference. Publication No. AREC 08-19, pp 25-35. Texas A&M University System.

McNeill, J.W., J.C. Paschal, M.S. McNeill and W.W. Morgan. 1996. Effect of morbidity on performance and profitability of feedlot steers. J. Anim. Sci. 74(Suppl.1):135.

Muggli-Cockett, N.E., L.V. Cundiff, and K.E. Gregory. 1992. Genetic analyses of bovine respiratory disease in beef calves during the first year of life. J. Anim. Sci. 70:2013-2019.

NAHMS. 2000. National Animal Health Monitoring System. Highlights of NAHMS Feedlot '99: Part II. USDA:APHIS:VS: NAHMS. Ft. Collins, CO.

NAHMS. 2013a. National Animal Health Monitoring System. Part I: Types and Costs of Respiratory Disease Treatments in U.S. Feedlots. USDA:APHIS:VS: NAHMS. Ft. Collins, CO.

NAHMS. 2013b. National Animal Health Monitoring System. Part II: Management Practices on U.S. Feedlots with a Capacity of Fewer than 1,000 Head. USDA:APHIS:VS: NAHMS. Ft. Collins, CO.

NAHMS. 2013c. National Animal Health Monitoring System. Part I: Management Practices on U.S. Feedlots with a Capacity of 1,000 or More Head. USDA:APHIS:VS: NAHMS. Ft. Collins, CO.

Noffsinger, T., and L. Locatelli. 2004. Low-stress cattle handling: An overlooked dimension of management. Pages 65-78 in Proc. Meet. Academy of Veterinary Consultants. Vol. XXXII, No 2. Colorado Springs, CO.

Perino, L. J. 1997. Advances in pulmonary immunology. Vet. Clin. North Am. Food Anim. Pract. 13:393-399.

Peterhans, E., T.W., Jungi, and M. Schweizer, 2003. BVD and innate immunity. Biologicals. 31:107-111.

Ridpath, J.F., J.D. Neill. 2007. Impact of variation in acute virulence of BVD1 strains on design of better vaccine efficacy challenge models. J. Vaccine. 47:8058-8066.

Roeber, D.L., N.C. Speer, J.G. Gentry, J.D. Tatum, C.D. Smith, J.C. Whittier, G.F. Jones, K.E. Belk, and G.C. Smith. 2001. Feeder cattle health management: Effects on

morbidity rates, feedlot performance, carcass characteristics, and beef palatability. Prof. Anim. Sc. 17:39-44.

Roth, J. A., and L. M. Henderson. 2001. New technology for improved vaccine safety and efficacy. Vet. Clin. North. Am. Food Anim. Pract. 17(3)585-597.

Sandvik, T. 2005. Selection and use of laboratory diagnostic assays in BVD control programmes. Preventitive Veterinary Medicine 72:3-16.

Schneider, M.J., R.G. Tait Jr., W.D. Busby, and J.M, Reecy. 2009. An evaluation of bovine respiratory disease complex in feedlot cattle: impact on performance and carcass traits using treatment records and lung lesion scores. J. Anim. Sci. 87:1821-1827.

Smith, R.A. 1998. Impact of disease on feedlot performance: A review. J. Anim. Sci. 76:272-274.

Snowder G.D., L.D. Van Vleck, L.V. Cundiff and G.L. Bennett. 2005. Influence of breed, heterozygosity, and disease incidence on estimates of variance components of respiratory disease in preweaned beef calves. J. Anim. Sci. 83:1247–1261.

Snowder G.D., L.D. Van Vleck, L.V. Cundiff and G.L. Bennett. 2006. Bovine respiratory disease in feedlot cattle: Environmental, genetic, and economic factors. J. Anim. Sci. 84:1999-2008.

Sowell, B. F., M. E. Branine, J. G. P. Bowman, M. E. Hubbert, H. E. Sherwood, and W. Quimby. 1999. Feeding and watering behavior of healthy and morbid steers in a commercial feedlot. J. Anim. Sci. 77:1105-1112.

Step, D. L. C. R. Krehbiel, L. O. Burciag-Robles, B. P. Holland, R. W. Fulton, A. W. Confer, D. T. Bechtol, D. L. Brister, J. P. Hutchison, and H. L Newcomb. 2009. Comparison of single vaccination versus revaccination with a modified live virus vaccine containing bovine herpesvirus-1, bovine viral diarrhea virus (1a and 2a), parainfluenza type 3 virus, and bovine respiratory syncytial virus in the prevention of bovine respiratory disease in cattle. J. Am. Vet. Med. Assoc. 235(5):580-587

Thompson, P. N., A. Stone, and W. A. Schultheiss. 2006. Use of treatment records and lung lesion scoring to estimate the effect of respiratory disease on growth during early and late finishing periods in South African feedlot cattle. J. Anim. Sci. 84:488-498.

Wilson, S.H. 1989. Why are meaningful field trials difficult to achieve for bovine respiratory disease vaccines? Can. Vet. J. 30:299-302

Wittum, T. E., N. E. Woollen, L. J. Perino, and E. T. Littledike. 1996. Relationships among treatment for respiratory tract disease, pulmonary lesions evident at slaughter, and rate of weight gain in feedlot cattle. J. Am. Vet. Med. Assoc. 209:814-818.