Innovations in Animal Health Diagnosis

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WT RESEARCH FEEDLOT

FEEDING QUALITY FORUM

CERTIFIED ANGUS BEEF BRAND

Overview

- Traditional Diagnostic Methods
- Novel Diagnostic Methods
- Implementation Challenges
- Targeted Metaphylaxis
- Conclusions

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Photo: Dr. Eben Oosthuysen

- Clinical signs are subjective
- Herd/Prey Instinct of cattle is problematic
- Currently, BRD diagnosis is a learned art, not a science (Edwards, 2010)
- Experienced pen riders are vital, but increasingly limited

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THE WALL STREET JOURNAL.

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BUSINESS

Cowboys Turn to High-Tech Ear Tags to Monitor Animal Health

Sensors that track livestock health may offer a way to reduce antibiotics used in meat production

Cattle at the Johnson Livestock feedlot in Idaho Falls, Idaho, wore high-tech ear tags earlier...

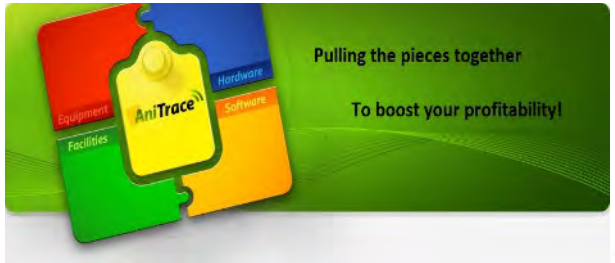
GrowSafe SYSTEMS®

QUANTIFIEDAG®

AAD Information that counts® Advanced Animal Diagnostics

REDI Remote Early Disease Identification

SCR by Allflex Make every cow count



WHISPER®

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Behavior Assessment for BRD Diagnosis

- Physical Behavior
  - IceQube
  - SCR by Allflex
- Eating/Drinking Behavior
  - GrowSafe
  - Advex
- Spatial Behavior
  - REDI System

Physical Behavior

- Advantage
  - Differential behavior variables
  - Greater Se/Sp?

- Disadvantage
  - Dairy focus
  - Difficult to install
  - Too big for beef calves
  - Misplacement
  - No BRD algorithm
  - No indicator on pedometer

Alteration of activity variables relative to clinical diagnosis of bovine respiratory disease in newly received feedlot cattle

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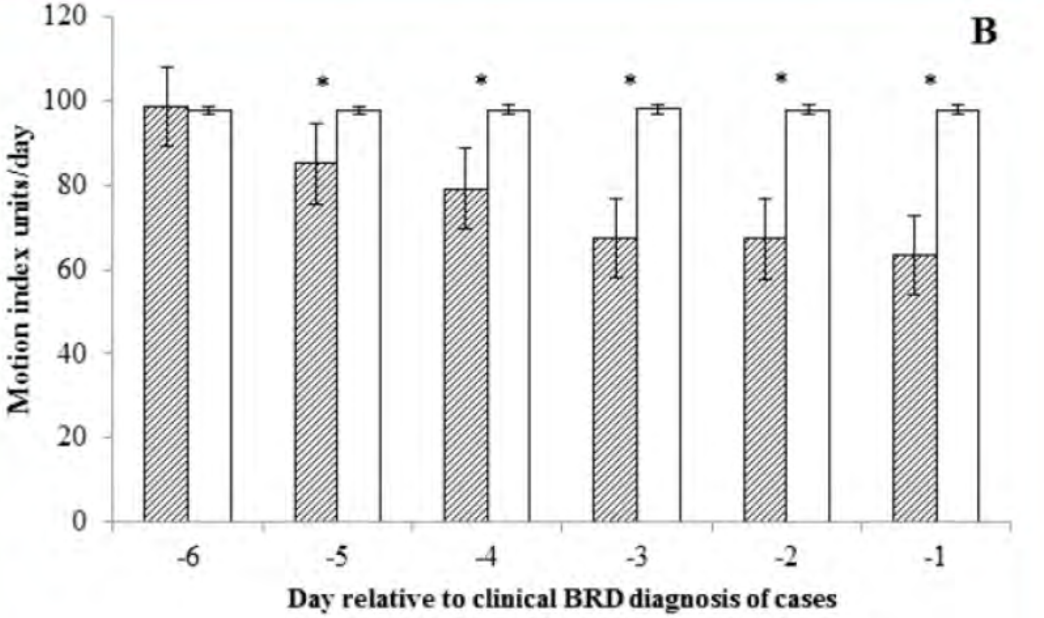
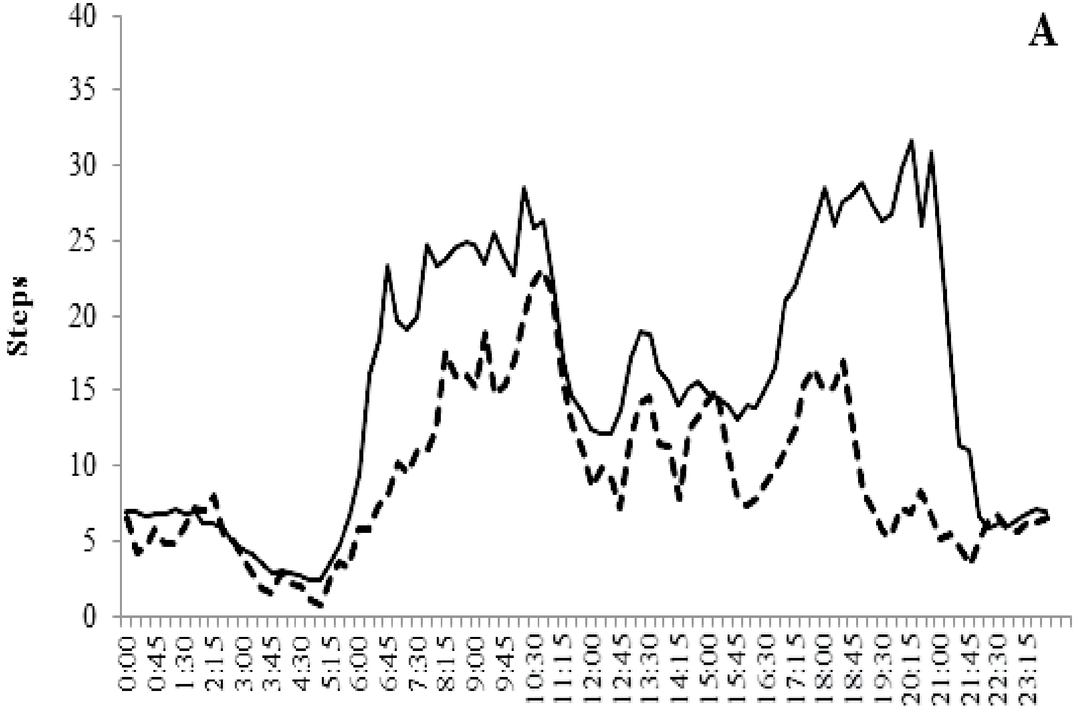
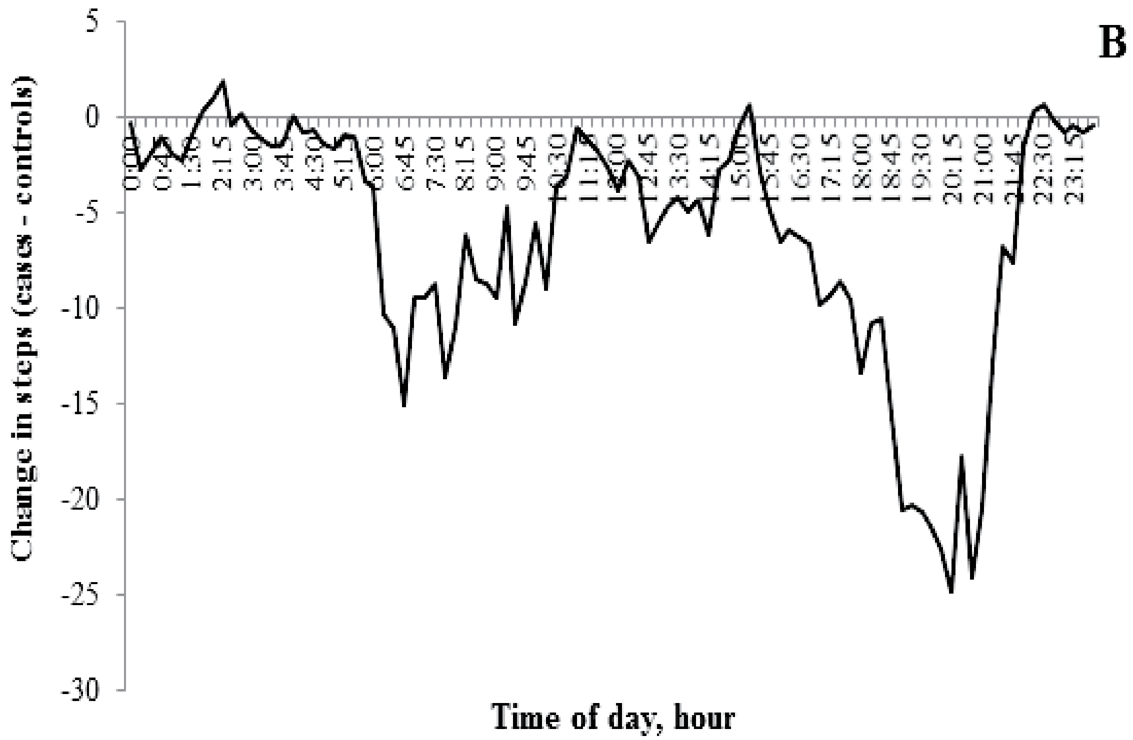


Figure 1. Average steps/day (A) and motion index units/day (B) for clinical bovine respiratory disease (BRD) cases and controls on the day relative to clinical BRD diagnosis in a commercial feedlot. Data were analyzed using the MIXED procedure of SAS with repeated measures and LSMEANS were generated. Effect of BRD status (A: $P < 0.001$; B: $P < 0.001$), day relative to clinical BRD diagnosis of cases (A: $P = 0.45$; B: $P = 0.99$), and their interaction (A: $P < 0.001$; B: $P < 0.001$) were tested. Statistical significance of means within a day relative to clinical BRD diagnosis is indicated with an asterisk, $P \leq 0.01$. Activity variables were determined from an accelerometer device[a] affixed proximate to the metatarsus of the right-rear leg.


A
Steps


B
Change in steps (cases - controls)
Time of day, hour

Physical Behavior

- Advantage
  - Easy to install and good retention
  - Rumination time and activity
  - Low infrastructure investment
  - Probably less expensive

- Disadvantage
  - Dairy/heat detection focus
  - No differential physical behavior
  - Misplacement
  - No BRD algorithm
  - No indicator on tag currently

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Make every cow count

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Oral hydration therapy with water and bovine respiratory disease incidence affects rumination behavior, rumen pH, and rumen temperature in high-risk, newly received beef calves

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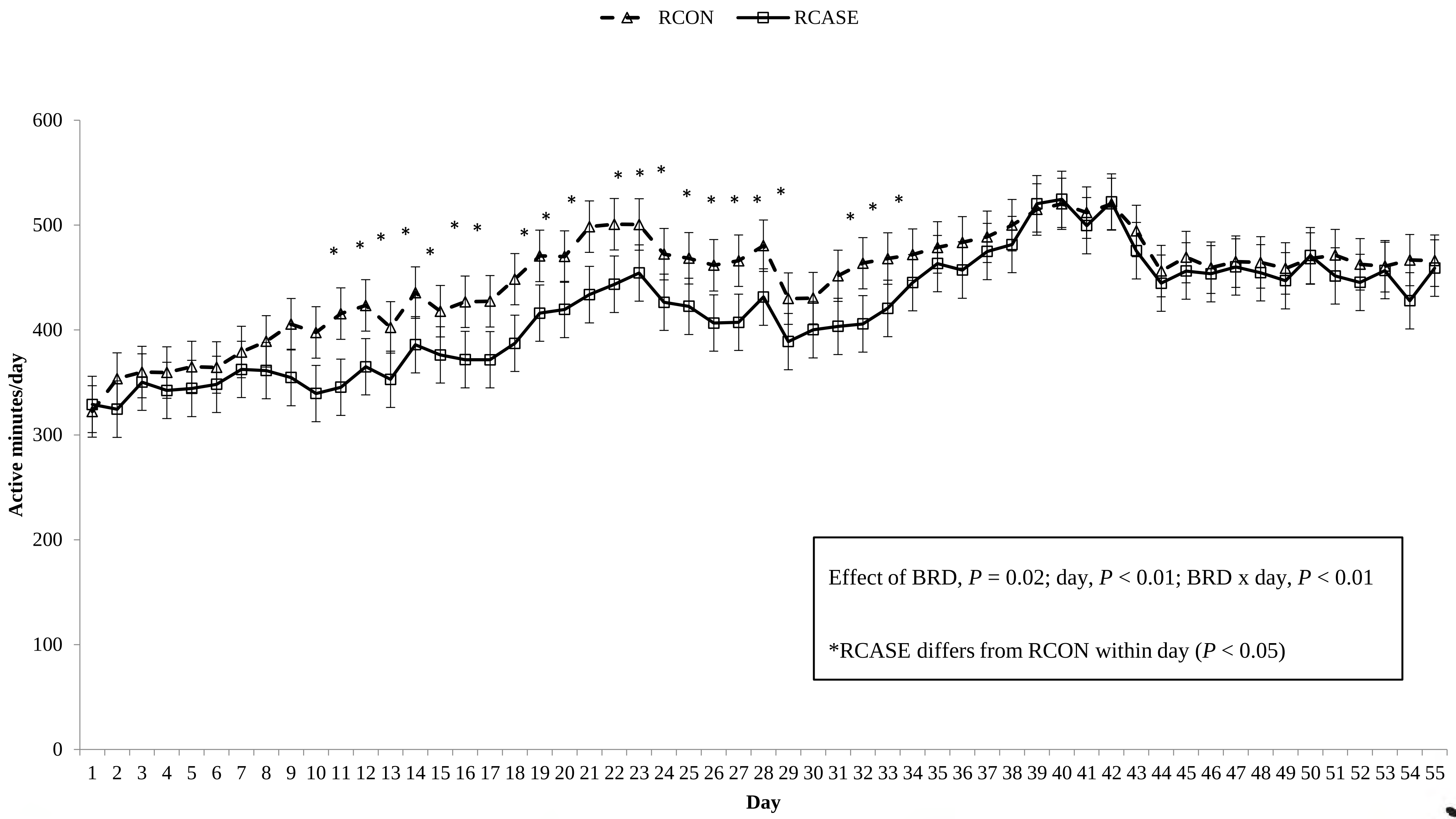
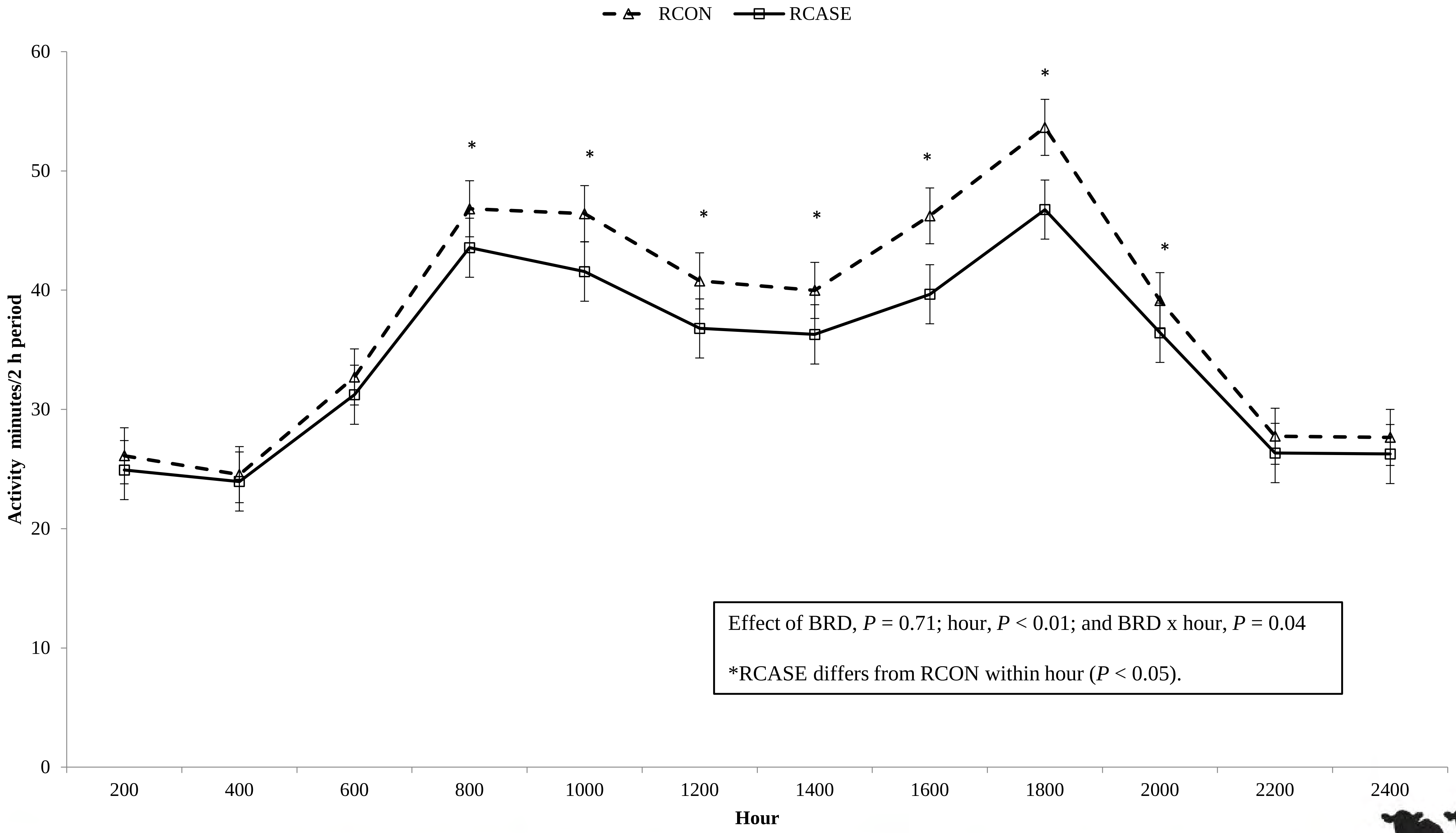
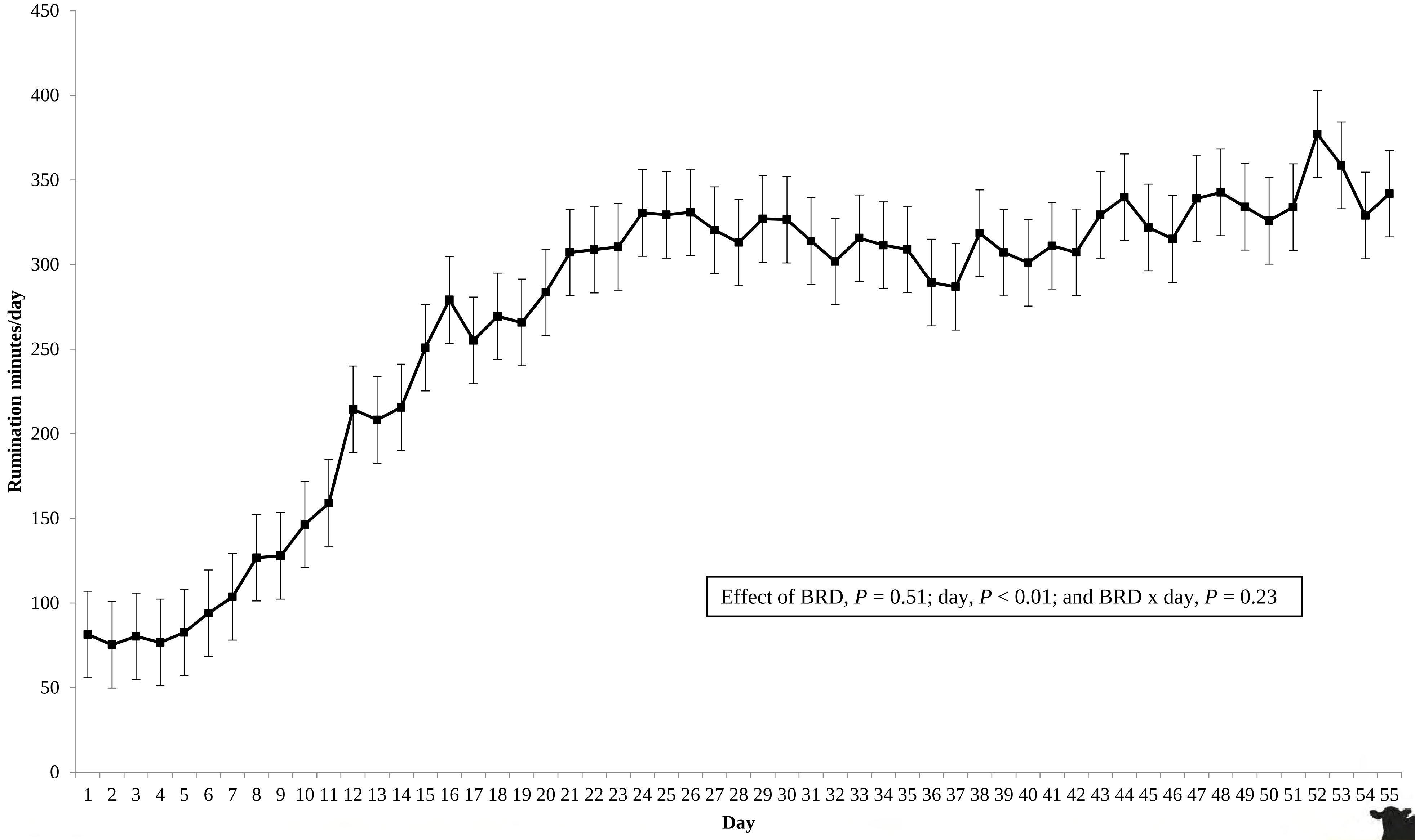
ABSTRACT: The study objectives were to determine the effect of oral hydration therapy and bovine respiratory disease (**BRD**) on rumination behavior, rumen pH, and rumen temperature. A random subset of high-risk, auction-sourced data from the accelerometer collar (n = 19 and 29) and rumen bolus (n = 12 and 21, for RCASE and RCON, respectively). Daily means and hourly means across days throughout the 56-d observation period were generated. Fixed effects

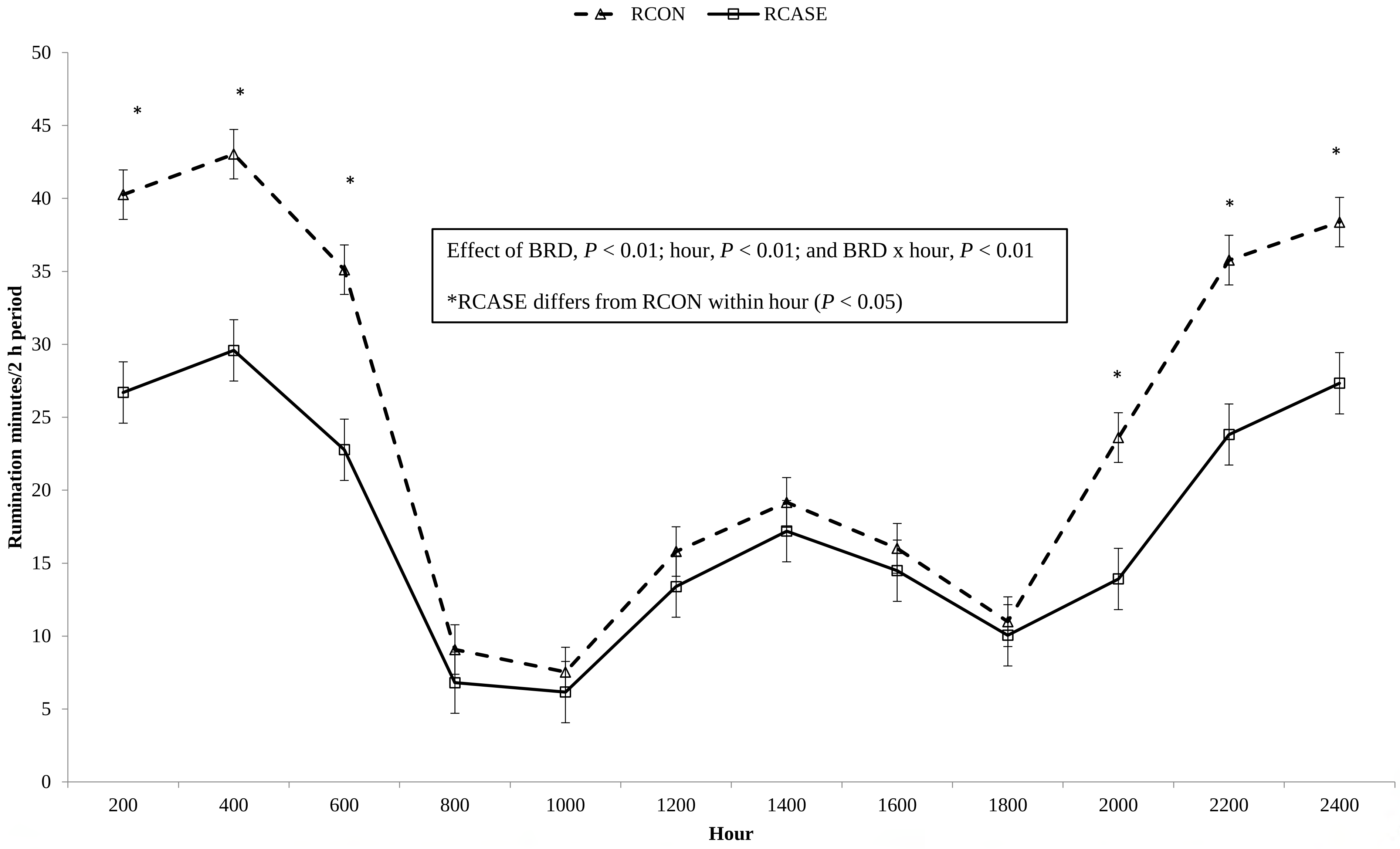

RCON
RCASE
Active minutes/day
600
500
400
300
200
100
0
Day
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55
Effect of BRD, P = 0.02; day, P < 0.01; BRD x day, P < 0.01
*RCASE differs from RCON within day (P < 0.05)



RCON
RCASE
60
50
40
30
20
10
0
Activity minutes/2 h period
*
200
400
600
800
1000
1200
1400
1600
1800
2000
2200
2400
Hour
Effect of BRD, P = 0.71; hour, P < 0.01; and BRD x hour, P = 0.04
*RCASE differs from RCON within hour (P < 0.05).



Rumination minutes/day
0
50
100
150
200
250
300
350
400
450
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55
Day
Effect of BRD, P = 0.51; day, P < 0.01; and BRD x day, P = 0.23


RCON
RCASE
Rumination minutes/2 h period
Hour
Effect of BRD, P < 0.01; hour, P < 0.01; and BRD x hour, P < 0.01
*RCASE differs from RCON within hour (P < 0.05)
0
5
10
15
20
25
30
35
40
45
50
200
400
600
800
1000
1200
1400
1600
1800
2000
2200
2400
*
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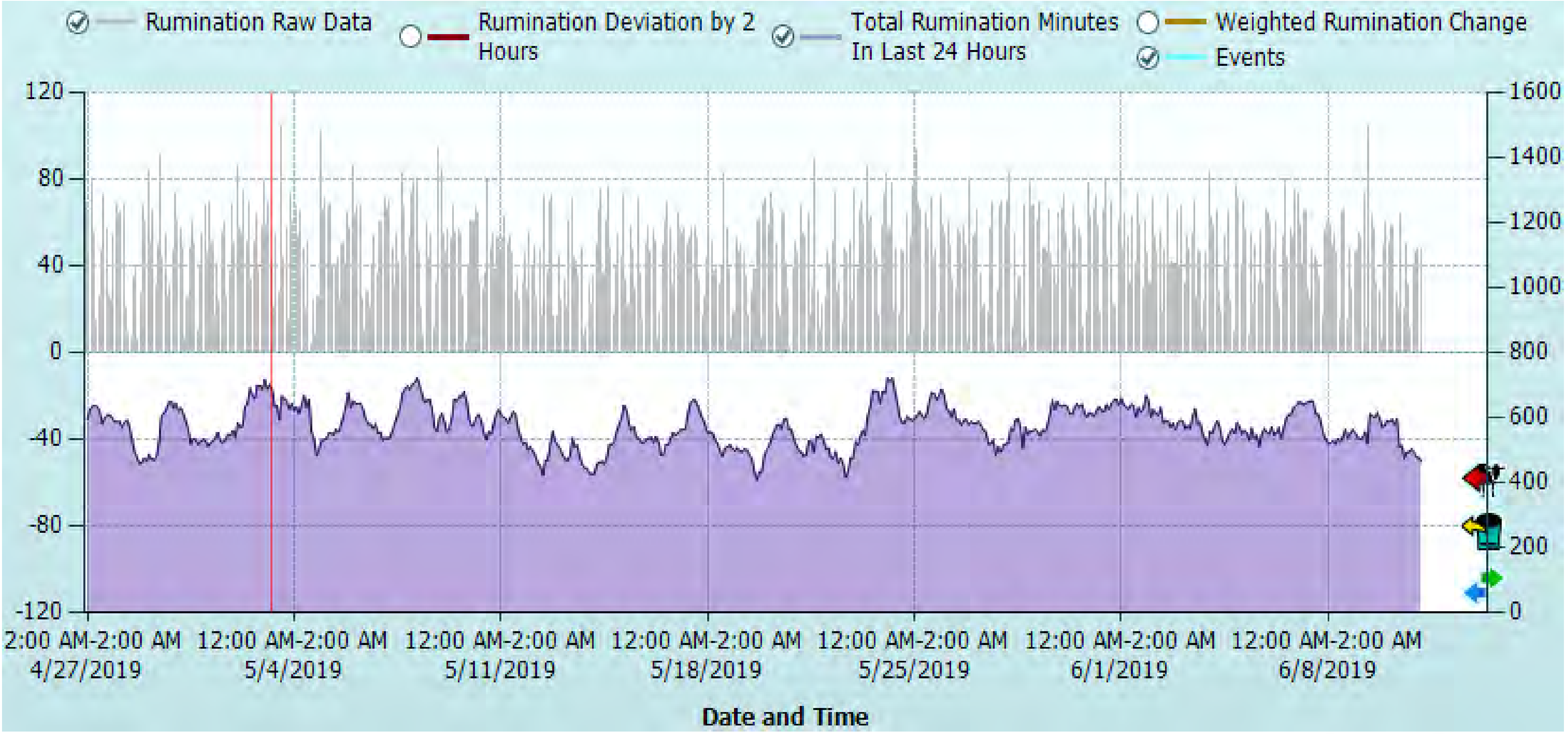
SCR Ear-tag Case Study

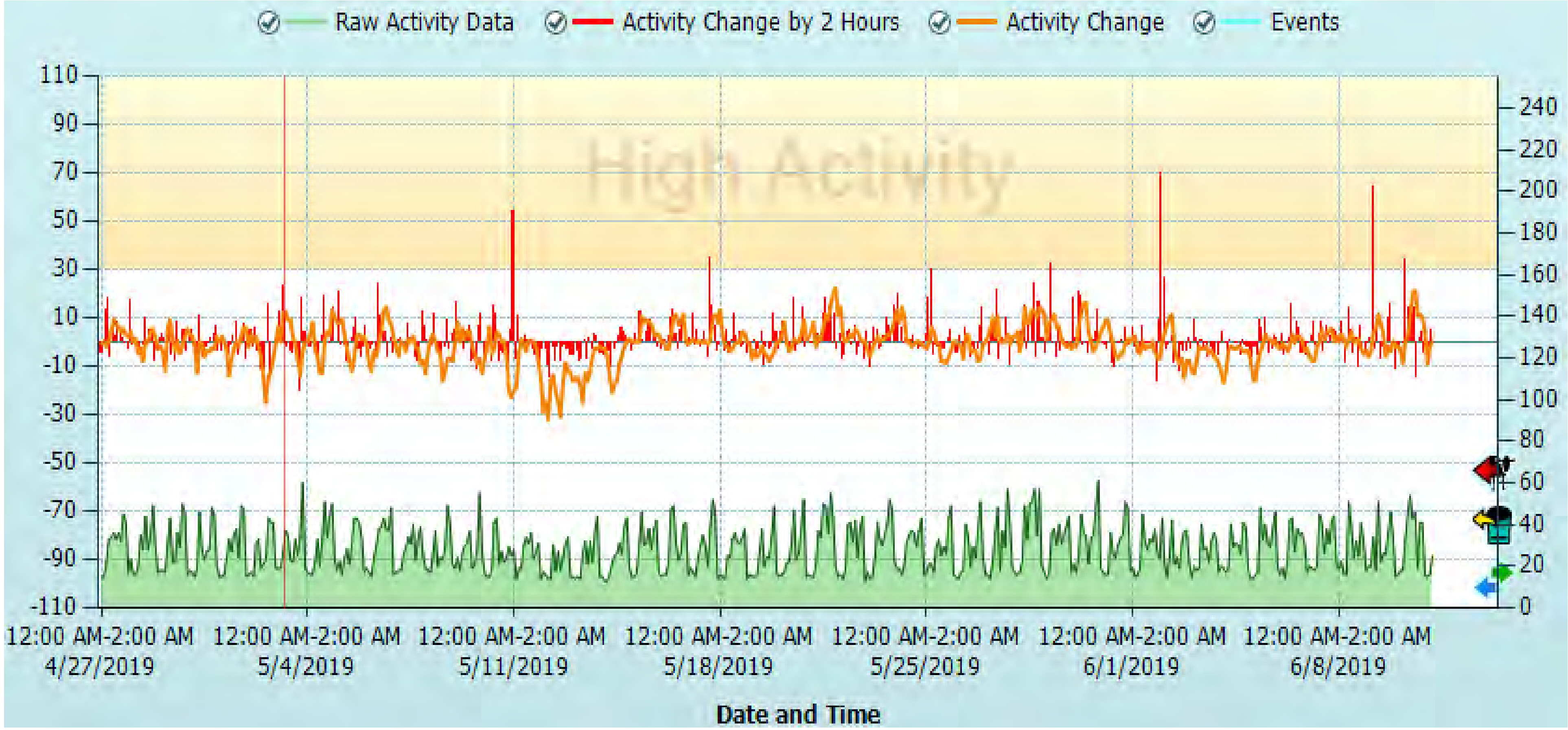
<u>Healthy animal</u>

- Steer ID 530
- No SCR system health alerts
- Not treated for any health problems

ID 530 – Rumination



ID 530 – Activity

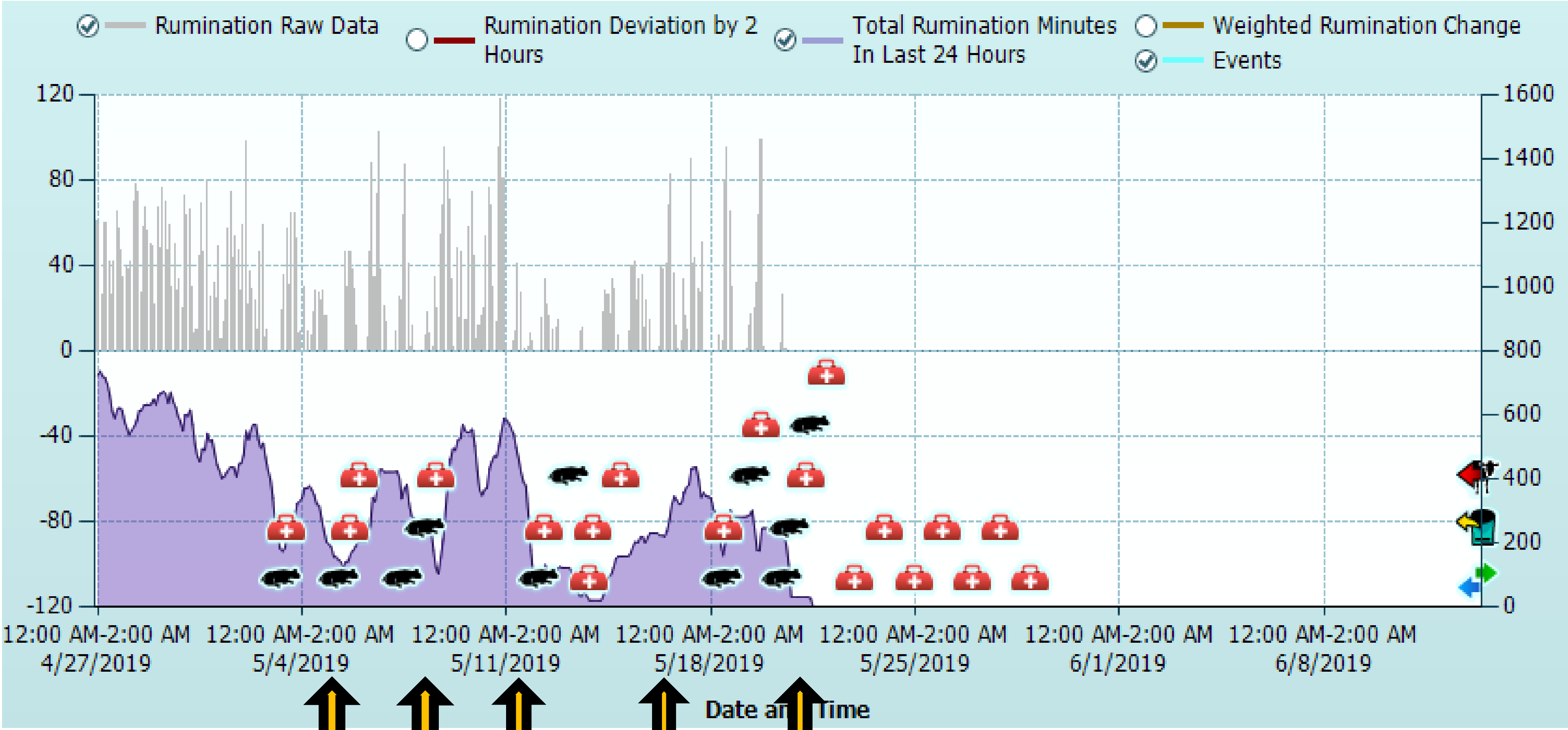


SCR Ear-tag Case Study

Chronic animal

- Steer ID 738
- Numerous SCR system health alerts
- Treated for BRD 4 times
- Died, necropsy revealed severe pleurisy and bronchopneumonia (BRD)

ID 738 – Rumination



BRD1 – 6th May

BRD2 – 9th May

BRD3 – 12th May

BRD4 – 17th May

Died – 21st May

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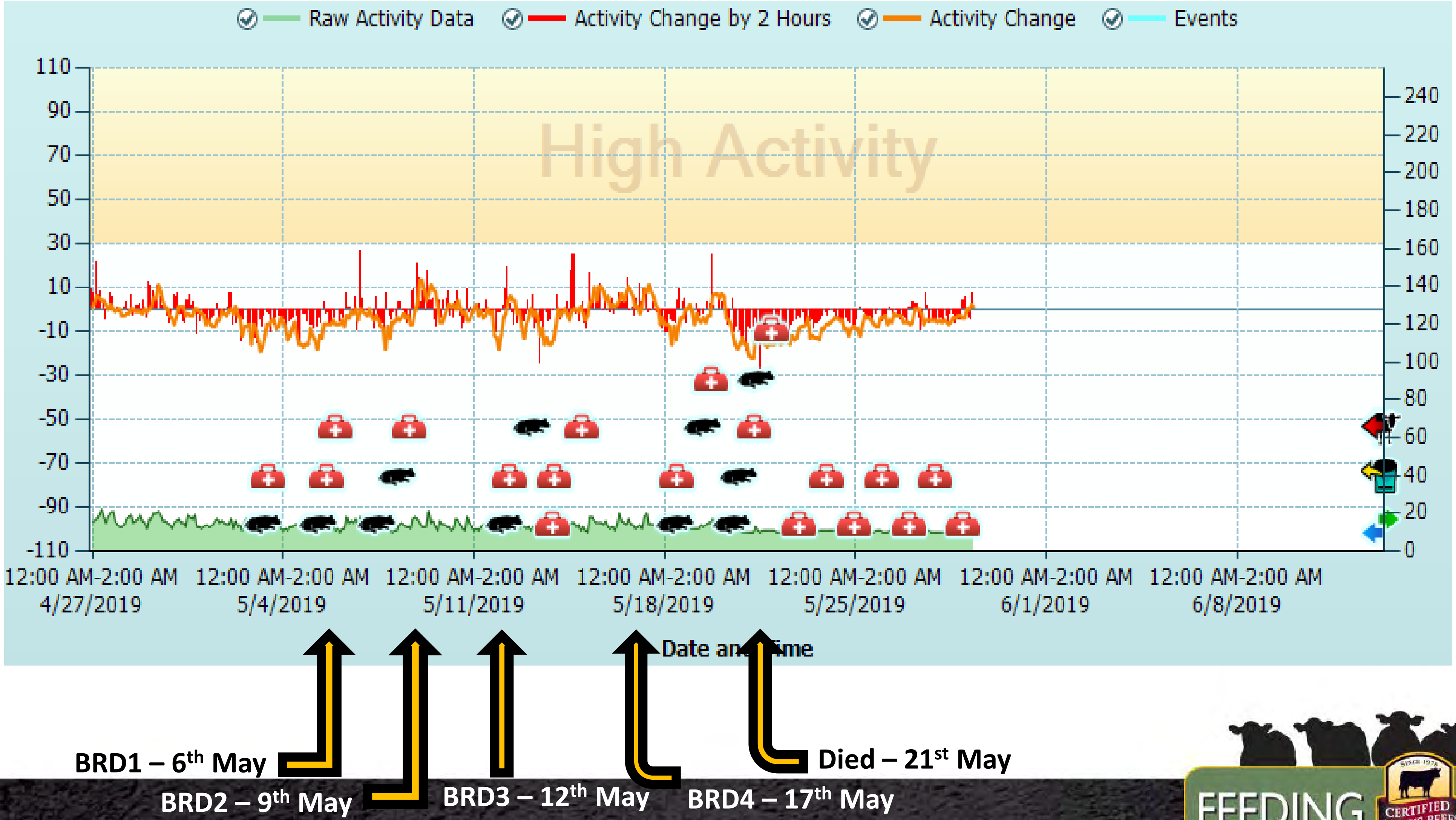
ID 738 – Activity



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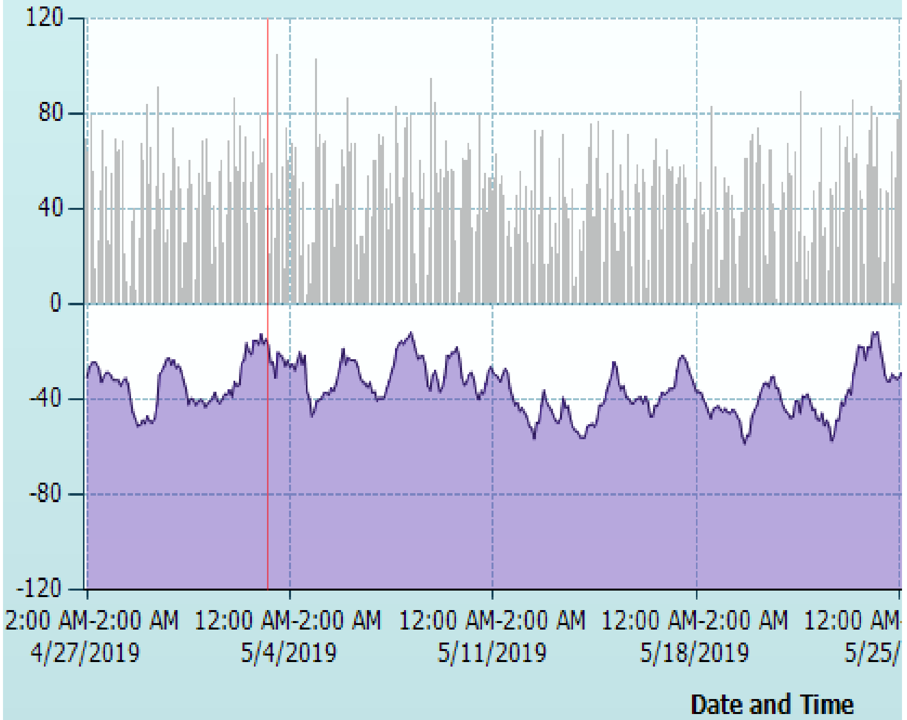
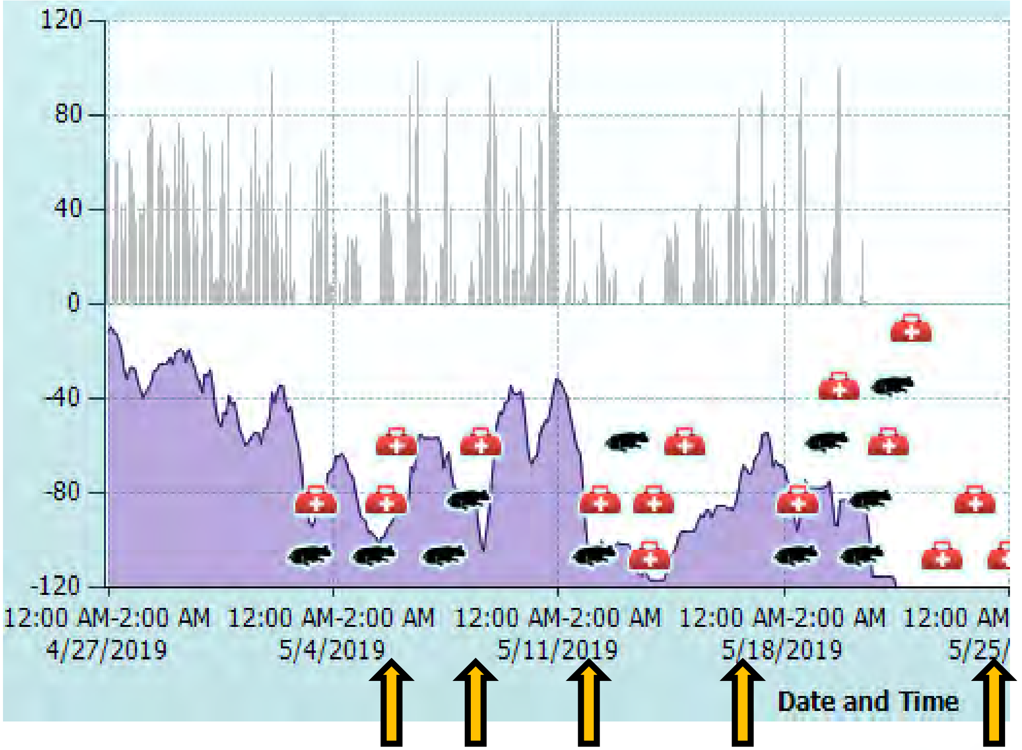
Comparison – Rumination

Healthy – ID 530



- Rumination pattern very consistent

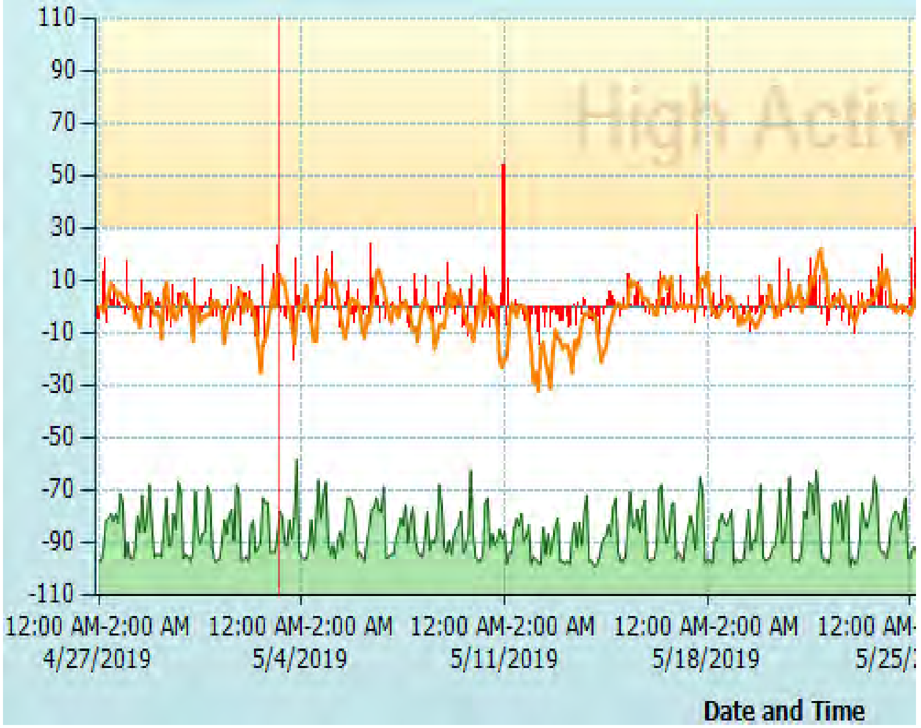
Chronic – ID 738



- Rumination pattern irregular
- Rumination lows coincide with Ab treatments
- Rumination ceased ~ 1 day before death

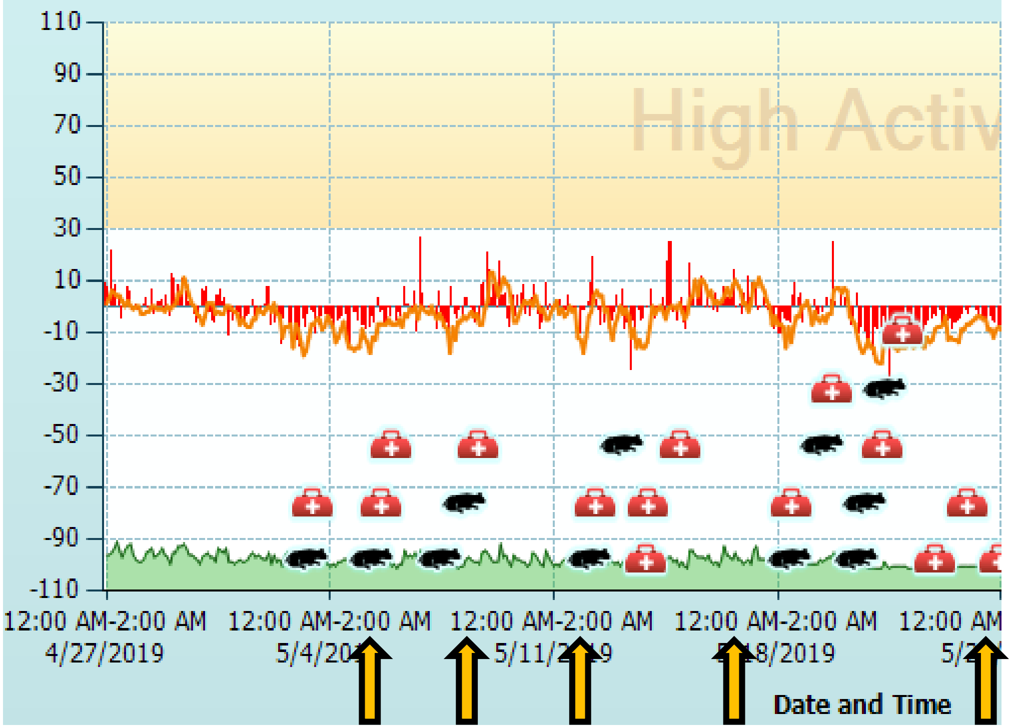
Comparison – Activity

<u>Healthy</u> – ID 530



- Maintained consistent diurnal activity pattern

<u>Chronic</u> – ID 738



- Maintained consistently low/static activity pattern

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Eating/Drinking Behavior

- Advantage
  - Tag cost probably less
  - Sick cattle don’t eat
  - Cattle that don’t eat get sick
  - Cattle that die stand at the water tank
- Disadvantage
  - Infrastructure investment
  - Alteration of bunk design
  - More hardware to maintain (and fail)

Spatial Behavior

- Advantage
  - Provides the most information
    - Physical
    - Feeding/Watering
    - Spatial
  - Contact patterns
  - Feedlot focus

- Disadvantage
  - High infrastructure investment
  - More hardware to maintain (and fail)
  - Transponder coverage is limited

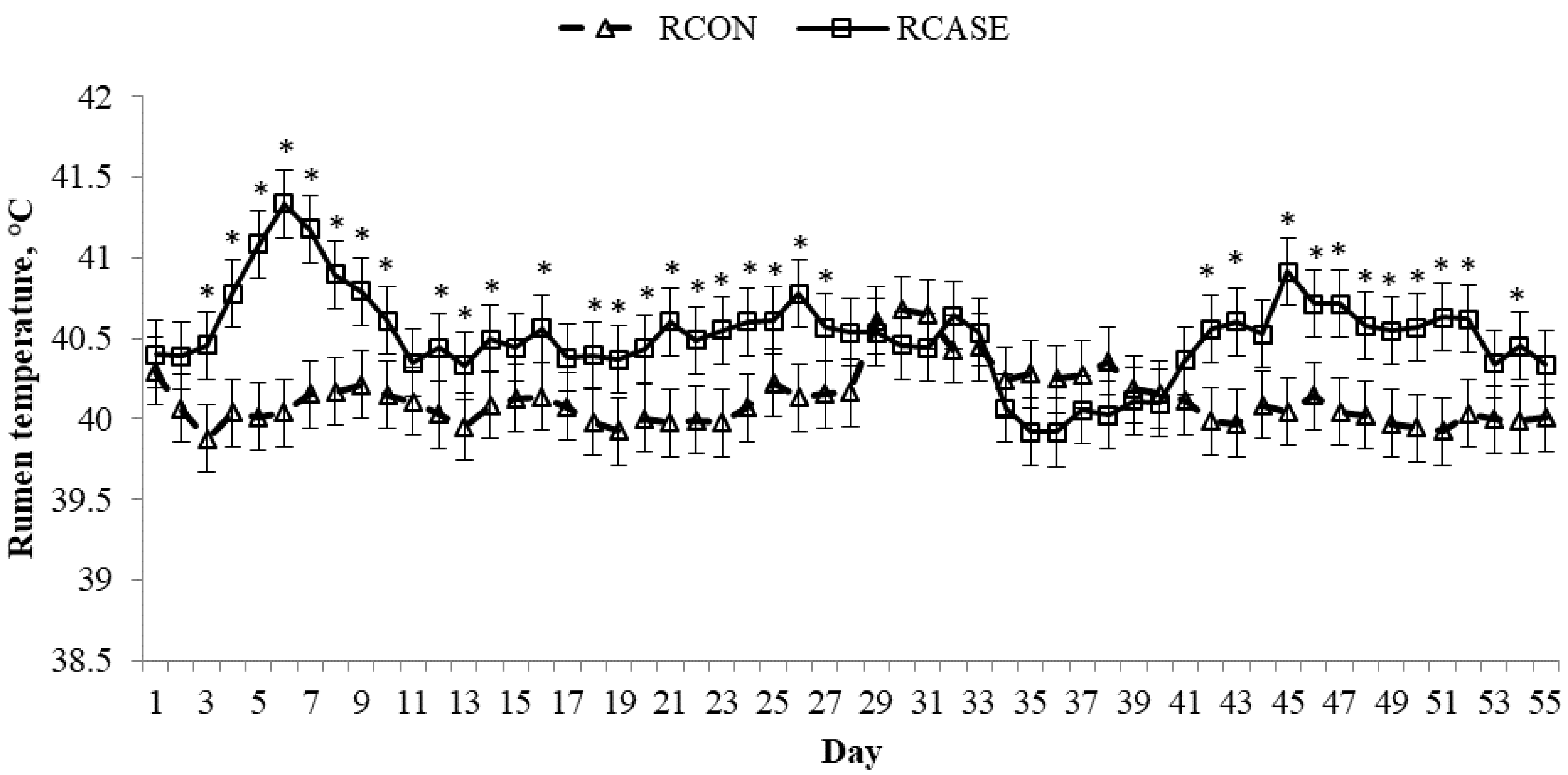
For more on the different cattle behavior technology…

- Richeson et al. (2018) Trans. Anim. Sci.
- Wolfger et al. (2015) Vet. Clin. N. Am. Food Anim. Pract.
- Theurer et al. (2013) Vet. Clin. N. Am. Food Anim. Pract.

Continuous Tympanic/Rumen Temperature

- Advantage
  - Alternative to behavior
  - Physiological
  - More direct indication of infection?

- Disadvantage
  - Bolus is a deal breaker
  - Ambient temperature effects
  - Installation



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Return on Investment

- If overall BRD morbidity is the same (or greater) where is the ROI?
  - Lower relapse rate
  - Lower mortality rate
  - Improved performance/COG
  - Enhanced labor structure

Return on Investment

Table 1. Theoretical health and economic outcomes of traditional vs. novel BRD diagnostic systems[1].

	Traditional	Novel	Cost Difference for Novel
BRD morbidity, %	40	55	$375.00
Relapse rate, %	40	30	-$250.00
Respiratory mortality, %	5	3	-$1,600.00
Novel system cost/animal, $	-	10.00	$1,000.00
Theoretical ROI, $[2]	-	4.25	$475.00

[1]Assumes sensitivity of 61.8% for traditional (White and Renter, 2009) and 75% for novel in 100 head lot size with average treatment cost of $25.00/animal and average death loss cost of $800.00/animal.

[2]Based on 100 animal lot size and assumes $10.00/animal total investment cost for novel implementation. Example does not consider performance or closeout differences between systems.

Implementation Challenges

- Requires individual animal identification
- Feedyard management must recognize benefit
- Pen rider acceptance (list vs. signal)
- Data management (lots and lots of data)
- Various BRD case definitions are possible
  - Give pen riders flexibility to pull on their own!

Targeted Metaphylaxis

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What is Targeted Metaphylaxis?

- *An Oxymoron:*
- Jumbo Shrimp
- Deafening Silence
- Exact Estimate
- Clearly Confused
- Found Missing
- Microsoft Works


Miracle cure kills fifth patient

By The Associated Press

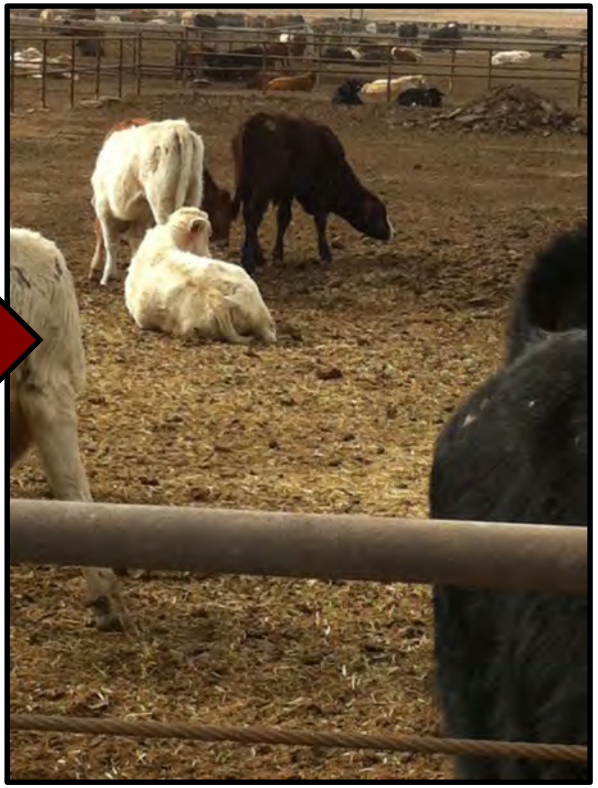
What is Targeted Metaphylaxis?

- **Metaphylaxis** is the timely mass medication of a group of animals to minimize an expected outbreak of disease (Edwards, 2010)
  - 92.6% use in high-capacity feedlots, to cattle <700 lb (Feedlot 2011, USDA)
  - *“The only thing we do at initial feedlot processing that has consistently shown to improve health outcome in medium- and high-risk cattle”* -Richeson

- **Targeted metaphylaxis** is an alternative disease control strategy applied at the individual animal level using a risk metric(s) as a decision tool (Richeson, 2018)

- Must be rapid, repeatable and accurate (but not perfect) and must have ROI

Population to individual basis



Absolute risk reduction (ARR)
Number needed to treat (NNT)

Number Needed to Treat (NNT)

- Regarding efficacy of antimicrobial metaphylaxis to control BRD:
  - ARR = c/c+d – a/a+b

(ARR = 0.5 – 0.25 = 0.25)

  - NNT = Reciprocal of ARR

(NNT = 1/0.25 = 4)

2 x 2 table	**BRD case, n=**	**“Healthy” control, n=**
Metaphylaxis	25 (a)	75 (b)
Non-metaphylaxis Control	50 (c)	50 (d)

Antimicrobial Effects and Bovine Respiratory Disease 109

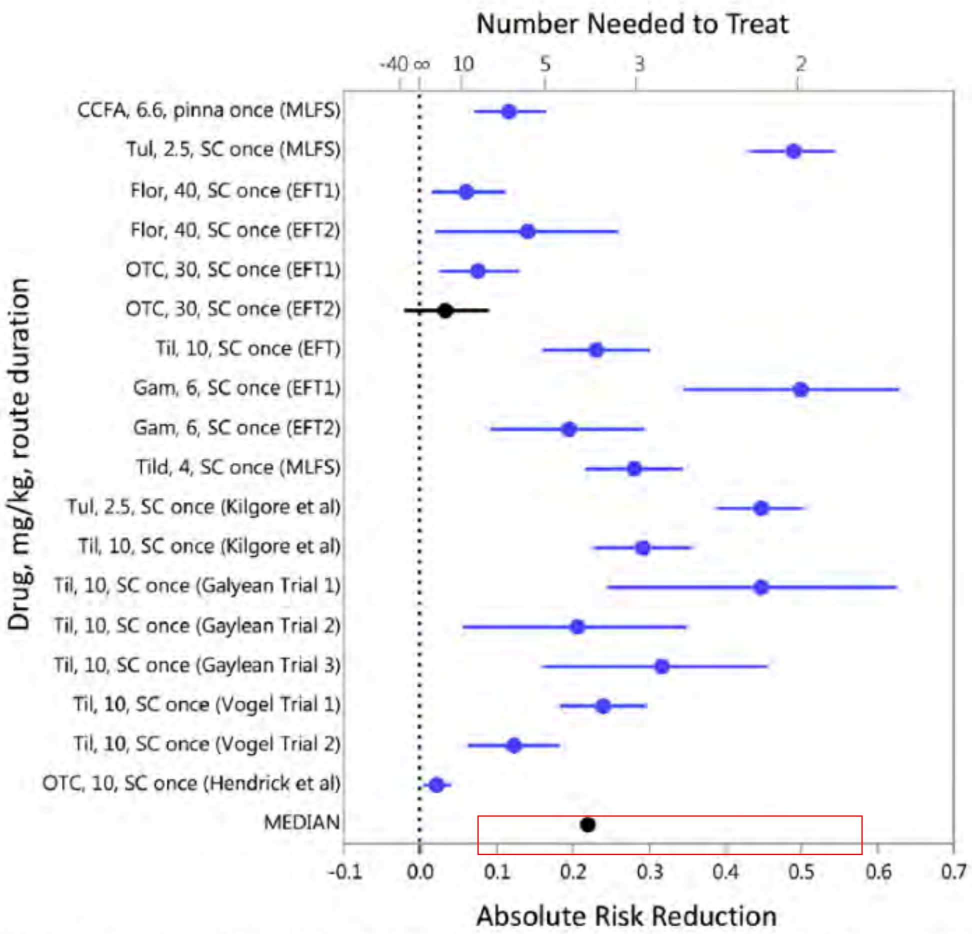


Fig. 8. Forest plot of point estimates and 95% CIs of the ARR (*bottom X axis*) and the corresponding NNT (*top X axis*) found from analysis of the control studies. Studies listed on the Y correspond in order to those listed in Table 1 and are listed by active ingredient, dose (mg/kg), route of administration, and duration of therapy. CT, clinical trial.

For BRD control studies, the median number of animals that need to be treated metaphylactically to prevent 1 acute case of BRD is **5** (DeDonder and Apley, 2015)

Thus, in a 100-head truckload administered metaphylaxis, only 20 head have a clinical benefit from the practice (on average)

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Why Targeted Metaphylaxis?

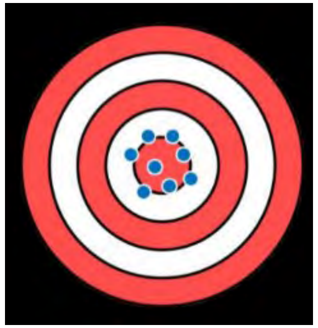
- Potential cost savings to the producer:
  - The cost of the test, labor and throughput to determine individual-animal candidates must be ≤ the amount saved on metaphylactic drug cost
  - The health and performance outcomes (really closeouts) for targeted metaphylaxis must be equivalent or improved
- Improved health management
- Address antimicrobial resistance concerns
- Demonstrate antimicrobial stewardship to our customers!

Targeted metaphylaxis strategies

- How can we target the “20 head” that clinically benefit from antimicrobial metaphylaxis?

Accuracy vs. Precision

- Accuracy = ability to provide a true measure of the subsequent BRD risk



- Precision = ability to provide a consistent test result (even if it is wrong)

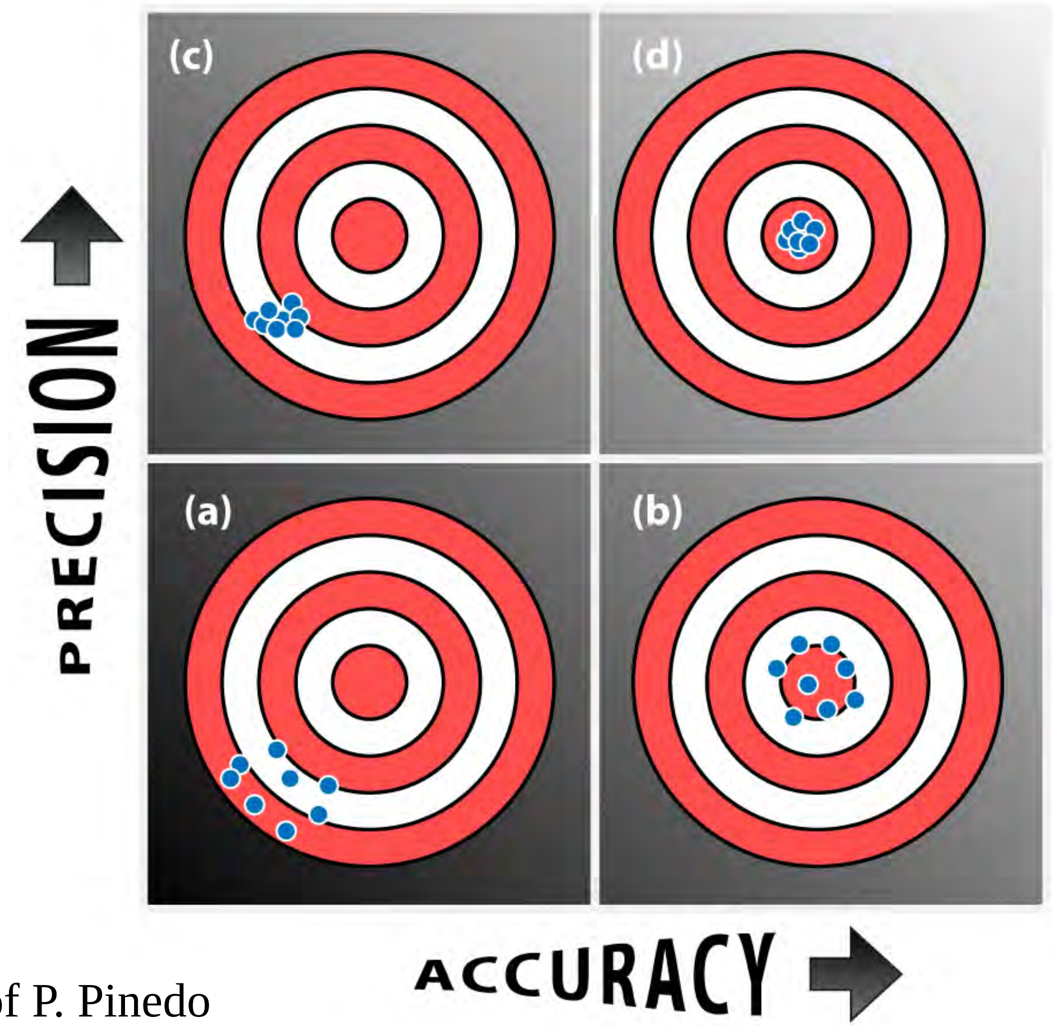


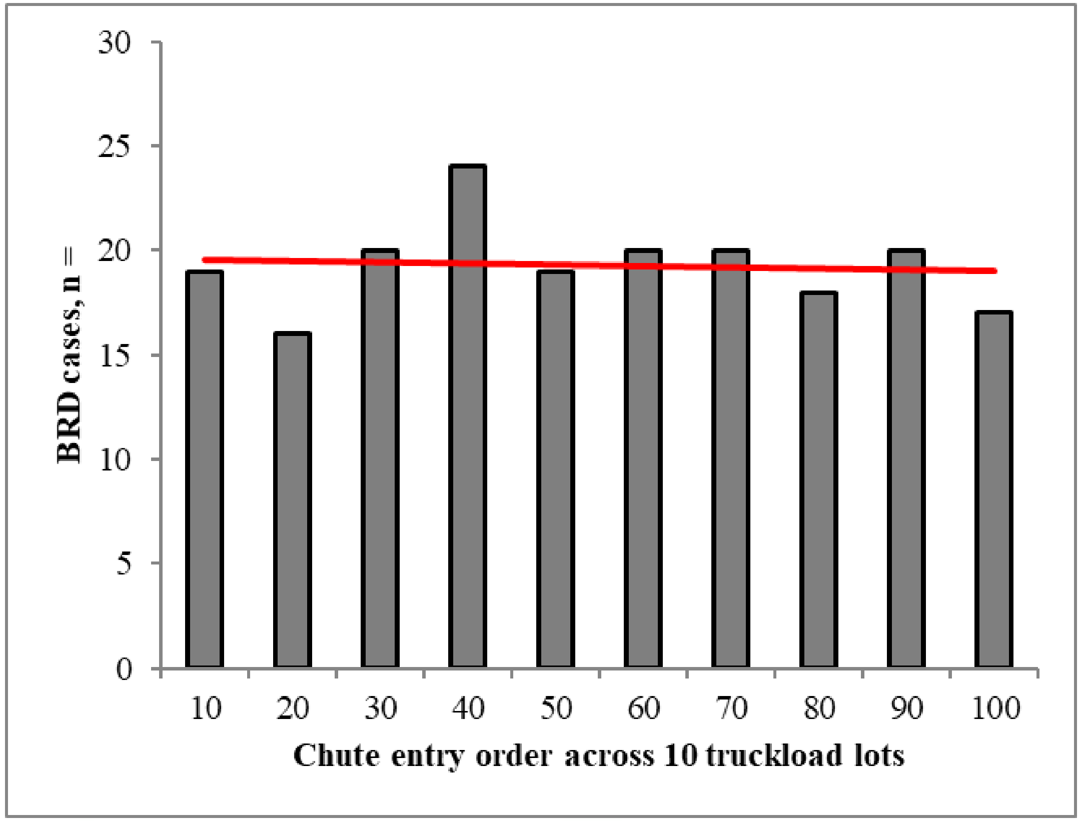
Image courtesy of P. Pinedo

Targeted metaphylaxis strategies

- Remember…rapid, repeatable, and accurate (and cheap) - must be “chute-side”

1. Chute entry order
2. Bulls vs. steers
3. Existing ear-tag
4. BW relative to cohorts
5. Rectal temperature
6. Lung auscultations
7. **Biomarker-assisted**

1. Chute entry order at initial processing



Unpublished data, WTAMU Research Feedlot

2. Bulls vs. steers at arrival

- The odds of clinical BRD in stocker calves that arrived as bulls were 3.32 times the odds of BRD for steers (Richeson et al., 2013)

- Castration pre-disposes calves to BRD
  - Pain and inflammation
  - Infectious complications
  - Immune taxation

3. Existing ear-tag at arrival

- Richeson hypothesis – the odds of BRD in auction market calves that arrive without an existing ear tag are greater than those that arrive with an existing ear tag
  - Association ≠ Causation

- Evidence that the animal has been handled at least once
  - Vaccinated, dewormed, weaned, better nutrition?
- Cattle that arrived with a pre-existing ear-tag were treated for BRD less often (*P* = 0.02; 25.2 vs. 37.6 %; Munoz et al., 2019).

4. Body weight relative to cohorts

- Lighter BW within truckload = increased BRD risk ($P \leq 0.06$; Pillen et al., 2016)

Arrival BW quartile	BRD morbidity, %
Lightest (<25%)	50.7[a]
Intermediate (26 to 75%)	44.8[b]
Heaviest (> 75%)	38.7[c]

5. Rectal temperature

- Rectal temperature ≥39.7°C at initial processing
- Trial 3 in Galyean et al. (1995)

Experimental treatment (n = 4)	BRD morbidity, %	Day 0 to 56 ADG, kg/d
Control (0%)	43.6[a]	1.42[a]
Mass (100%)	11.9[b]	1.57[b]
Temp (39.7°C; 41.9% qualified)	12.9[b]	1.56[b]

5. Rectal temperature

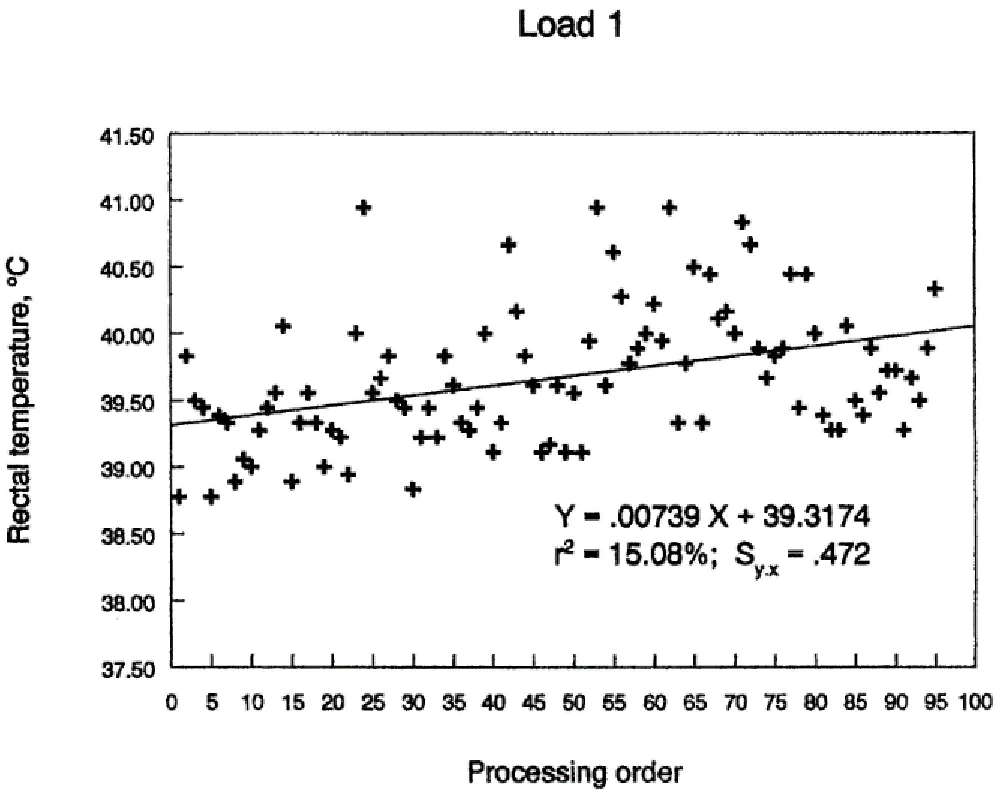


Figure 1. Relationship between processing order and rectal temperature at the time of arrival processing of newly received beef cattle in Load 1 of Trial 3.

6. Lung auscultation

- Manual is highly subjective, poor precision
- Whisper Electronic Stethoscope

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7. Biomarker-assisted variables

- Haptoglobin
- Serum non-esterified fatty acid (NEFA) or other serum chemistry variables
- Nasal microbiome signatures
- Leukocyte profile
  - Complete blood count variables (Richeson et al., 2013)
  - QScout® BLD (Advanced Animal Diagnostics)

Targeted metaphylaxis strategies

- Serum haptoglobin concentration
  - Acute-phase protein, synthesized by hepatocytes
  - Non-specific indicator of inflammatory status

Wittum et al. (1996) and Burciaga-Robles et al. (2009) suggest poor correlation between serum haptoglobin concentration at clinical BRD treatment

In: Roberts et al., 2018

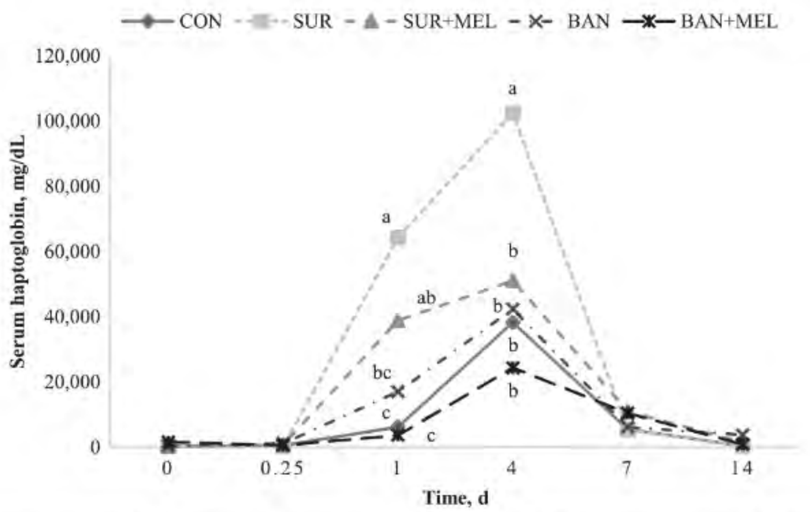


Figure 1. Effect of castration method and meloxicam administration on serum haptoglobin concentration (mg/dL) of feedlot cattle. Effect of treatment, $P = 0.05$; day, $P < 0.001$; and treatment × day, $P = 0.04$. Contrasts = method, $P = 0.01$; meloxicam, $P = 0.13$; interaction, $P = 0.52$; and CON vs. castrates, $P = 0.21$. [abc]Least square means with uncommon superscript letters differ within day, $P < 0.05$.

Targeted metaphylaxis strategies

- NEFA concentration
  - Indicative of lipolysis, negative energy balance

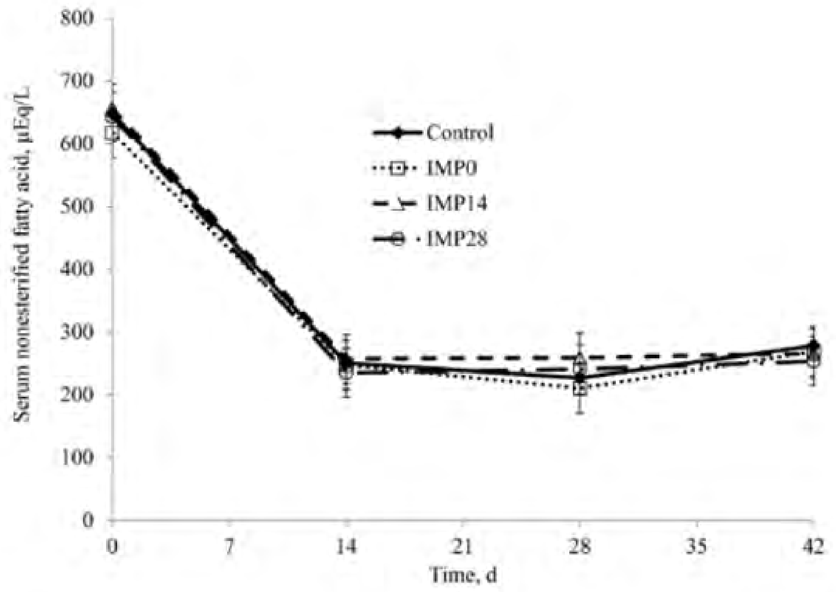
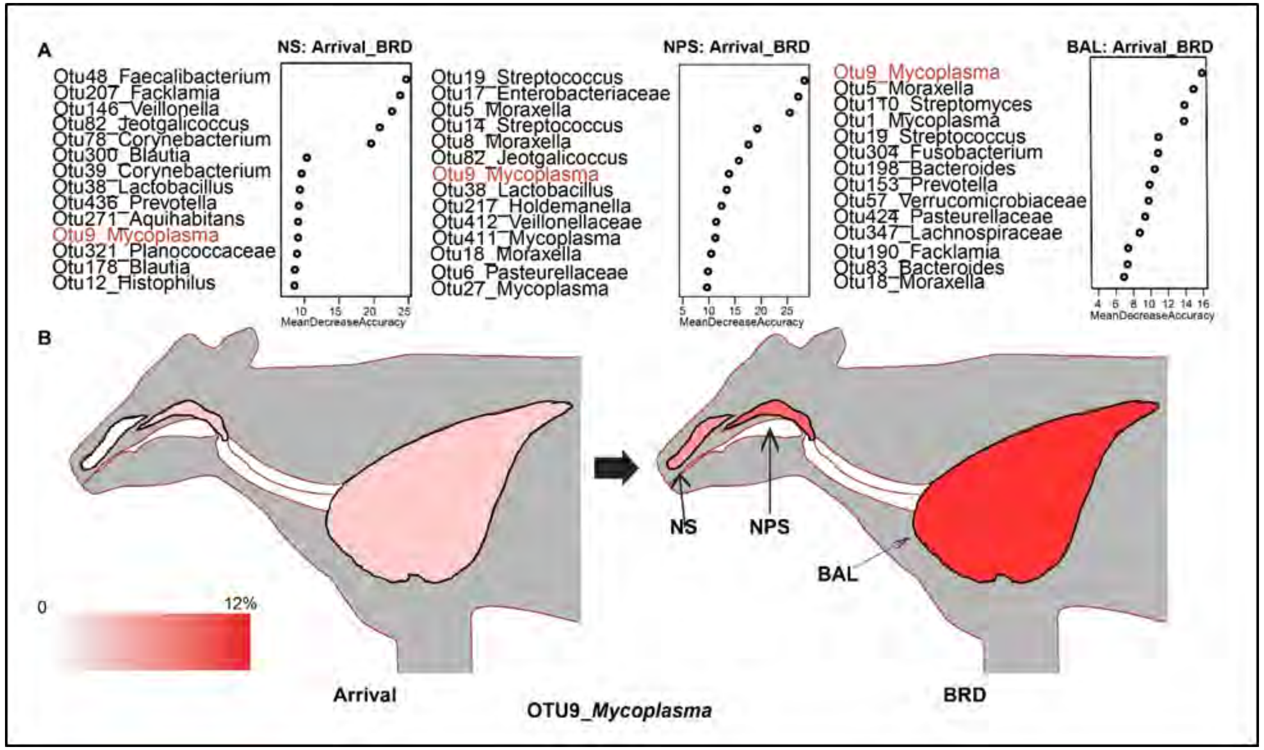


Figure 2. Effect of timing of growth implant administration on serum NEFA of newly received beef calves. Control = no growth implant administered; IMP0 = growth implant administered on d 0; IMP14 = growth implant administered on d 14; IMP28 = growth implant administered on d 28. Treatment, $P = 0.82$; day, $P < 0.0001$; treatment × day, $P = 1.00$.

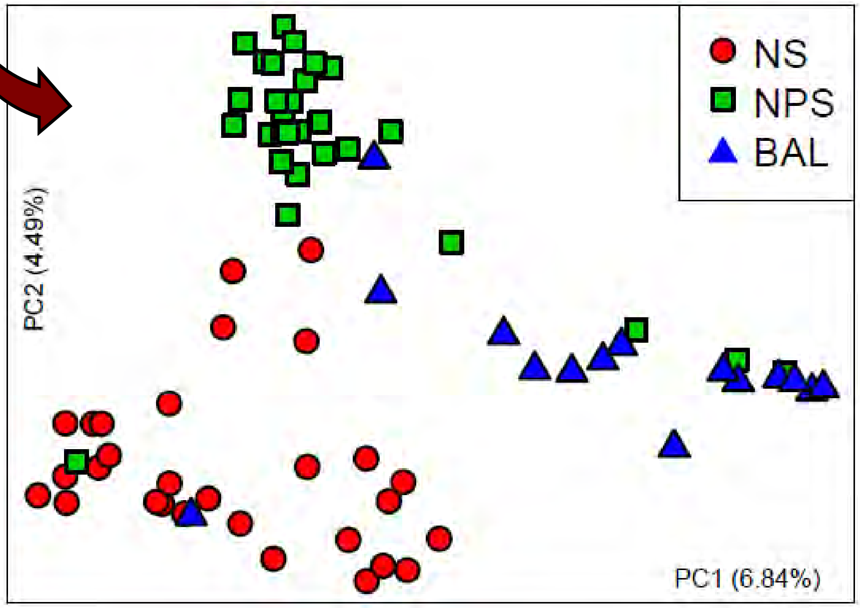
In: Richeson et al. (2015)

Targeted metaphylaxis strategies

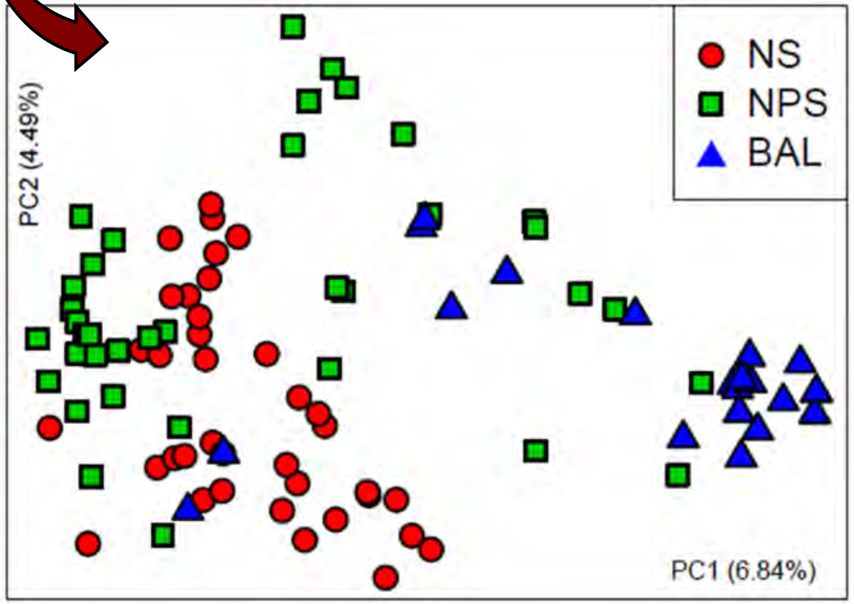
- Nasal microbiome signatures



Biogeography of the bovine respiratory microbiome in <u>clinically healthy beef cattle</u>



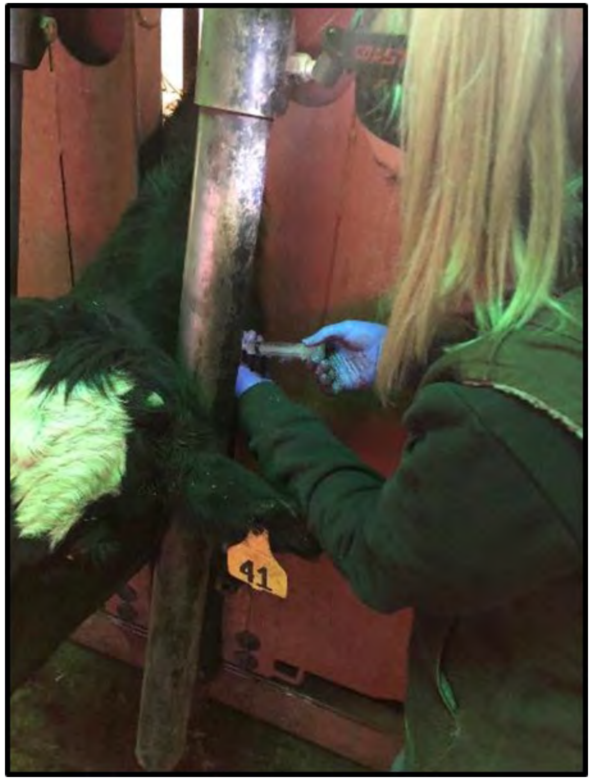
Biogeography of the bovine respiratory microbiome in <u>beef cattle clinically diagnosed with BRD</u>



Chai et al., in preparation for ISME journal

Targeted metaphylaxis strategies

- Leukocyte profile
- Richeson et al. (2013)



Association of hematologic variables and castration status at the time of arrival at a research facility with the risk of bovine respiratory disease in beef calves

John T. Richeson, PhD; Pablo J. Pinedo, DMV, PhD; Elizabeth B. Kegley, PhD; Jeremy G. Powell, DVM, PhD; M. Shane Gadberry, PhD; Paul A. Beck, PhD; Shollie M. Falkenberg, PhD

RUMINANTS

Objective—To determine the association of CBC variables and castration status at the time of arrival at a research facility with the risk of development of bovine respiratory disease (BRD).

Design—Retrospective cohort study.

Animals—1,179 crossbred beef bull (n = 588) and steer (591) calves included in 4 experiments at 2 University of Arkansas research facilities.

Procedures—Calves underwent processing and treatments in accordance with the experiment in which they were enrolled. Castration status and values of CBC variables were determined at the time of arrival at the facilities. Calves were monitored to detect signs of BRD during a 42-day period.

Results—The areas under the receiving operator characteristic curves for CBC variables with significant contrast test results ranged from 0.51 (neutrophil count) to 0.67 (eosinophil count), indicating they were limited predictors of BRD in calves. The only CBC variables that had significant associations with BRD in calves as determined via multivariable logistic regression analysis were eosinophil and RBC counts. The odds of BRD for bulls were 3.32 times the odds of BRD for steers.

Conclusions and Clinical Relevance—Results of this study indicated that low eosinophil and high RBC counts in blood samples may be useful for identification of calves with a high risk for development of BRD. Further research may be warranted to validate these variables for prediction of BRD in calves. Calves that were bulls at the time of arrival had a higher risk of BRD, versus calves that were steers at that time. (*J Am Vet Med Assoc* 2013;243:1035–1041)

Table 4—Results of multivariable logistic regression analysis for an association between values of various CBC variables and the risk of BRD for calves during a 42-day period after arrival at a research facility.

Variable	BRD1 OR	BRD1 95% CI	BRD1 *P* value	BRD2 OR	BRD2 95% CI	BRD2 *P* value
2-level categorization						
Eosinophils (X 10^3 cells/μL)			< 0.001			< 0.001
< 0.054	1.98	1.31–2.89		2.04	1.41–2.97	
≥ 0.054	—	—		—	—	
RBCs (X 10^6 cells/μL)			0.058			0.03
< 10.0	0.75	0.49–1.01		0.69	0.49–0.97	
≥ 10.0	—	—		—	—	
3-level categorization						
Eosinophils (X 10^3 cells/μL)			0.002			< 0.001
< 0.011	2.65	1.54–4.57		2.51	1.51–4.17	
0.011–0.108	1.55	0.99–2.41		1.71	1.07–2.73	
> 0.108	—	—		—	—	
RBCs (X 10^6 cells/μL)			0.002			0.007
< 9.46	0.62	0.36–1.05		0.63	0.41–0.98	
9.46–11.2	0.44	0.28–0.70		0.53	0.36–0.79	
> 11.2	—	—		—	—	

Only CBC variables with significant ($P \leq 0.05$) effects on determination of a diagnosis of BRD at least once in calves are included.

— = Referent.

See Table 3 for remainder of key.

Targeted metaphylaxis strategies

- 1 + 1 = 3? – Synergy with multiple variables included in a prediction algorithm

- Technology already exists for multiple variables to “talk” and input data into complex prediction algorithm

- Binomial or ordinal test result?

Conclusions

- Each of the behavior assessment systems have shown promise for early BRD detection from limited, preliminary research

- There is still much more work to be done before widespread adoption in commercial feedlots
  - Algorithm development
  - Beta-testing
  - Cost:benefit
  - BRD case definitions

Conclusions

- Late-term BRD identification is probably much improved for novel behavior assessment systems

- Pen riders and cattle managers will need to be convinced and trained to use a different system

- Possible enhancement, probably not revolutionary
  - Benefit will vary from feedyard to feedyard and cowboy to cowboy

Conclusions

- Current antimicrobial metaphylaxis strategies will need to be refined
  - Cost benefit (reduced drug cost vs. targeted metaphylaxis cost)
  - Consumers are asking for less antimicrobial use
  - Government regulation?

- Several methods show potential, but continued research is needed

- Combination of methods into algorithm will likely be most predictive of subsequent BRD risk (maximum Sensitivity-Se/Specificity-Sp)
  - AI/Machine learning specific to individual feedlot

- Acceptance of technological inputs in a relatively conservative U.S. beef industry is a challenge

Thank you!

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