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Bayesian evaluation of clinical diagnostic test characteristics of visual observations and remote monitoring to diagnose bovine respiratory disease in beef calves

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ABSTRACT

Accurate diagnosis of bovine respiratory disease (BRD) in beef cattle is a critical facet of therapeutic programs through promotion of prompt treatment of diseased calves in concert with judicious use of antimicrobials. Despite the known inaccuracies, visual observation (VO) of clinical signs is the conventional diagnostic modality for BRD diagnosis. Objective methods of remotely monitoring cattle wellness could improve diagnostic accuracy; however, little information exists describing the accuracy of this method compared to traditional techniques. The objective of this research is to employ Bayesian methodology to elicit diagnostic characteristics of conventional VO compared to remote early disease identification (REDI) to diagnose BRD. Data from previous literature on the accuracy of VO were combined with trial data consisting of direct comparison between VO and REDI for BRD in two populations. No true gold standard diagnostic test exists for BRD; therefore, estimates of diagnostic characteristics of each test were generated using Bayesian latent class analysis. Results indicate a 90.0% probability that the sensitivity of REDI (median 81.3%; 95% probability interval [PI]: 55.5, 95.8) was higher than VO sensitivity (64.5%; PI: 57.9, 70.8). The specificity of REDI (median 92.9%; PI: 88.2, 96.9) was also higher compared to VO (median 69.1%; PI: 66.3, 71.8). The differences in sensitivity and specificity resulted in REDI exhibiting higher positive and negative predictive values in both high (41.3%) and low (2.6%) prevalence situations. This research illustrates the potential of remote cattle monitoring to augment conventional methods of BRD diagnosis resulting in more accurate identification of diseased cattle.

1. Introduction

Accurate diagnosis is crucial in an effective therapeutic program. Bovine respiratory disease (BRD) is one of the most frequent and expensive disease of beef calves post-weaning (USDA, 2013a). A variety of etiologic agents have been implicated as a part of the syndrome, and *Mannheimia haemolytica* is considered the most common bacterial pathogen (Griffin et al., 2010). Therapy for BRD commonly includes an antimicrobial, and almost all cattle (99.9%) treated for BRD in U.S. feedlots had an injectable antibiotic as part of initial BRD therapy (USDA, 2013a). Combining the BRD treatment protocol with the prevalence of BRD in feedlot cattle means that 13.4% of all cattle placed in U.S. feedlots were treated with an injectable antibiotic for initial BRD therapy; (USDA, 2013a) therefore, accurate diagnosis is critical to insure judicious use of antimicrobial agents.

Efficacious post-therapeutic outcomes require accurate, timely diagnosis combined with appropriate selection of treatment agents, and treatment failures can result in decreased performance and death loss leading to significant economic losses (Apley, 2006). Visual observation (VO) is the conventional method for BRD diagnosis, yet this method has been illustrated to have relatively low diagnostic sensitivity and specificity (White and Renter, 2009;

Abbreviations: BRD, bovine respiratory disease; NPV, negative predictive value; PI, probability interval; PPV, positive predictive value; REDI, remote early disease identification system; Se, sensitivity; Sp, specificity; VO, visual observation.

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Amrine et al., 2013). Several other diagnostic modalities have been evaluated to augment the diagnostic characteristics of VO including evaluation of blood parameters (Hanzlicek et al., 2010; Fraser et al., 2014), inflammatory proteins (Humblet et al., 2004; Nikunen et al., 2007; Bannikov, 2011) and assessment of changes in external body temperature (Schaefer et al., 2007). Despite investigation to improve BRD diagnostics, no other modality has been shown to be more effective or cost efficacious than VO.

The premise for VO of BRD is based on evaluation of subjective clinical signs of illness including depression and anorexia. Evaluation of these clinical signs at a single point in time is subjective and results in relatively poor agreement among observers (Amrine et al., 2013). However, technology exists to remotely monitor cattle behavior, and remote monitoring of changes in activity and feeding behavior has been associated with BRD status (White et al., 2012; Wolfger et al., 2015a). Limited work exists comparing costs (Wolfger et al., 2014) or performance (White et al., 2015) of remote monitoring systems to visual appraisal related to calf health, and due to the lack of a gold standard, no work exists comparing the diagnostic characteristics of the two modalities. The objective of this research is to employ Bayesian methodology to elicit diagnostic characteristics of conventional VO compared to remote early disease identification (REDI) to diagnose BRD in the absence of a gold standard.

2. Materials and methods

No gold standard exists for clinical diagnosis of BRD; therefore, Bayesian latent class analysis techniques (Hanson et al., 2003; Branscum et al., 2005) were employed to estimate diagnostic characteristics of REDI and VO in two separate populations. Data from trials directly comparing systems were used to populate the model and prior distributions were created from a combination of previous literature (VO) and a pilot trial (REDI).

2.1. Trial data comparing REDI and VO

Data for analysis were collected from two independent trials on separate populations of cattle comparing VO to REDI. Both trials were conducted in private research facilities using experienced animal care givers and under an existing animal care and use protocol. In both trials, cattle were visually observed once (Trial 1) or twice (Trial 2) daily by experienced personnel for signs of clinical BRD. Both trials also utilized the REDI (Remote Early Disease Identification, Precision Animal Solutions, LLC, Canton, MO) system to identify BRD. The REDI system continuously monitors cattle behavior with a real time location system (Smartbow, MKWE, Vienna, Austria) combined with algorithms designed to identify BRD (White et al., 2015).

Trial 1 was conducted at a drylot stocker facility in Missouri using beef calves deemed at high risk for BRD. Data were collected over four replications (total $n = 168$) using similar calves in each replicate (average weights (kg): 191.9, 187.6, 202.3, and 225.9). Upon arrival all calves were processed in a similar manner including vaccination for viral pathogens, and application of REDI monitoring tags. Calves were not treated with antimicrobial metaphylaxis upon arrival and the REDI system was used to make all therapeutic decisions. During this time period, calves were also observed daily by an experienced veterinarian (DRG). Calves illustrating signs of illness by VO were recorded, but not treated unless identified as ill by REDI. The calves were monitored for BRD using REDI and VO for 31–33 days post-arrival.

Trial 2 was conducted in a commercial feedlot in Alberta, Canada using beef calves deemed at moderate risk for BRD. Calves arrived over a 9 day period and were placed in a single pen ($n = 311$) for a monitoring period lasting 37 days past the arrival of the first group of calves. Upon arrival, all calves were processed in a similar manner including vaccination for viral pathogens, application of REDI monitoring tags, and administration of metaphylaxis (tulathromycin). After administration of metaphylaxis, the expected BRD risk was low. During the monitoring period, calves were observed twice daily by an experienced pen rider in addition to the REDI monitoring system. Cattle were treated using the feedyard treatment protocol if identified as ill by either REDI or VO.

2.2. Prior distributions

Beta distributions (BetaBuster version 1.0) were used to specify prior distributions of the probability of prevalence in each trial, and diagnostic characteristics (sensitivity, Se and specificity, Sp) of each modality. The Se and Sp for VO were based on Bayesian estimates from previous literature (White and Renter, 2009). The prior for VO Se was set with a mode of 61.8 and 95% confidence the Se was greater than 55.7, and the VO prior for Sp was set with mode of 62.8% and 95% confidence the Sp was greater than 60.0.

No published information exists on Se or Sp of REDI; however, an unpublished trial was available for evaluation. The trial was a matched case control study where BRD positive calves were identified and a randomly selected healthy control was selected for comparison. After meeting initial inclusion criteria, a necropsy was performed to determine final true status of each individual. The criteria for a calf called BRD positive was the presence of clinical signs of disease for two consecutive days, a rectal temperature >40 °C, and the existence of >7% pulmonary lesions. The case inclusion criteria for healthy cattle was that they had never been observed as ill while at the facility, had a rectal temperature <39.5 °C at examination, and <5% pulmonary lesions at necropsy. The trial resulted in selection of 9 BRD cases and 9 healthy calves. The REDI system correctly identified 8 of the 9 (88.8%) BRD positive calves and all 9 healthy cattle. As these numbers were relatively small, priors were set conservatively with wide distributions. The Se for REDI was set with a mode of 85.0 and 95% certainty that Se was greater than 50.0, and Sp for REDI was set with mode of 95.0 and 95% certainty that REDI Sp was greater than 50.0.

The prior prevalence for each population was based on estimates provided by the consulting veterinarian (Trial 1 = DRG; Trial 2 = CB) for each operation based on their experience with this type of cattle in these facilities. Trial 1 contained high risk stocker cattle which did not receive metaphylaxis and the estimated BRD prevalence mode was 35.0 with 95% certainty it was greater than 20.0 ($\beta(7.30, 12.71)$). Trial 2 contained lower risk calves that received metaphylaxis upon arrival and the estimated prevalence mode was 7.0 with 95% certainty the prevalence was less than 20.0 ($\beta(2.95, 26.96)$).

2.3. Statistical analysis

Posterior inferences were based on 100,000 iterations from each model after a burn-in of 10,000 iterations. Three chain models were utilized and convergence assessed by visual evaluation of density, quantile, autocorrelation, trace plots, and Brooks–Gelman–Rubin diagnostic for each parameter as previously described (Enoe et al., 2000).

Both REDI and VO evaluate similar biologic indices (behavior); therefore, independence of the diagnostic tests cannot be assumed (Gardner et al., 2000). Conditional dependence models were used to evaluate the relationship between the Se and Sp of the two diagnostic tests in both populations with potential dependence among diagnostic characteristics as previously described (Branscum et al., 2005). The models estimated Se and Sp for both diagnostic tests and the prevalence in each population; therefore, the positive and negative predictive values for each test in each population were