Interpreting Outcome Measures of Disease and Health in Cattle Research and Practice

P.A. Ospina[1], *DVM, MPH;* **D.V. Nydam**[2], *DVM, PhD;* **T.J. DiCiccio**[3], *PhD*
[1]*Department of Animal Science, College of Agriculture and Life Sciences, Cornell University, Ithaca, NY 14850*
[2]*Department of Population Medicine and Diagnostic Sciences, College of Veterinary Medicine, Cornell University, Ithaca, NY 14850*
[3]*Department of Social Science, Industrial and Labor Relations School, Cornell University, Ithaca, NY 14850*

Introduction

Evaluating the association between multiple predictor variables such as β-hydroxybutyrate (BHBA) and parity level on a dichotomous outcome such as a displaced abomasum or no displaced abomasum is common in dairy research and practice. The risk ratio (RR) can be estimated to evaluate the strength of the association, i.e., how likely the outcome is to happen based on the levels of the predictor variables. The purpose of this study is to outline an applied method for estimating the RR with PROC GENMOD using SAS software version 9.2. This estimate is preferred to the odds ratio (OR), which can sometimes overestimate the effect and can be difficult to interpret.

Materials and Methods

Data from a prospective cohort study of 1,318 Holsteins in the postpartum period (3-14 days-in-milk (DIM)), in 100 herds from the Northeast is used to demonstrate how to estimate the RR. Blood was collected from approximately 15 cows in each herd, and BHBA was measured. These sampled cows were followed-up to 30 DIM, and data on whether they developed a displaced abomasum, and/or ketosis, and/or metritis was collected. This was the dichotomous outcome of interest. Predictor variables were: 1) exposure to BHBA concentrations ≥ 10 mg/dL; 2) parity = 1 or ≥ 2; 3) the interaction between BHBA and parity; and 4) herd as a random effect. The risk ratio can be estimated with PROC GENMOD in SAS as follows:

```
proc genmod descending data=work. BHBAstudy;
class herd BHBA Parity;
model Disease = BHBA Parity BHBA*Parity
/ link=log dist=Poisson pscale;
repeated subject = herd/ type = exch;
lsmeans BHBA10 * Parity / pdiff;
run;
```

Poisson regression can be used to estimate the risk ratio when counts represent the number of events that occurred over an observed period of time, and the time at risk is similar between all subjects. This type of analysis is done by specifying the Poisson distribution, with a log link function after the forward slash in the model statement. The pscale option corrects the standard errors for overdispersion, which occurs when the variance is larger than the mean, a major assumption of the Poisson distribution. The repeated statement, with the exchangeable matrix option, uses a class variable (e.g., herd) to cluster individual samples (e.g., cows). This clustering is done because it is reasonable to suspect that there will be more similarities among cows within the same herd versus those between herds, due to unmeasured characteristics of each herd. The "lsmeans/pdiff" line of code produces information about all of the permutations of the categorical variables in the interaction term.

Results

When an interaction is included in the model, there is no longer one single estimate that describes the effect of the covariates included in the interaction term; it now depends on the level of the second variable. The output generated from the "lsmeans/pdiff" option can be used to estimate the RR. Interpretation is as follows: the risk of developing any of the three diseases when BHBA was ≥ 10 mg/dL and parity was =1 (compared to a cow with BHBA < 10 mg/dL) was 6.7; however, this same cow has 8.5 greater odds of developing the outcome of interest than a cow with BHBA < 10 mg/dL. In cows (parity ≥2) the risk ratio of developing the outcome of interest was 3.7 when BHBA was ≥10 mg/dL compared to a cow with BHBA <10 mg/dL; however, the odds ratio for this same comparison was 4.3. In both models, RR and OR, BHBA was a significant covariate (P<0.0001), parity was not (P>0.25), and the interaction term had a low chance of a type I error (P=0.08).

Significance

The OR can sometimes over-estimate the effect and can be difficult to interpret. Therefore, the approach for estimating the RR may be used in both cohort studies and randomized trials when there is a yes or no outcome. Estimating the likelihood of disease will allow for effective prevention aimed at improving the health of dairy cows.