

A simulation method to reconstruct the longitudinal animal and herd level infection status based on repeated screening tests with no gold standard: application to paratuberculosis modeling

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As gold-standard tests are not always available, evaluating the performance of imperfect tests is important to determine the infection status of animals regularly screened for disease. Although methods to evaluate performance of tests with binary outcomes exist, no methods are available to determine multiple infection states from longitudinal data such as fecal culture and ELISA tests for *Mycobacterium avium* subsp. *paratuberculosis* (MAP). The parameters from infectious disease models (IDM) are often estimated from such test results. Yet, the joint uncertainty in the test results is rarely considered. The objective of this study was to develop a method to estimate the confidence on the animal level infection progression using longitudinal screening test results, and use the results to estimate IDM parameters. Test results from a paratuberculosis control program were used to demonstrate the method. The results of 12,957 parallel fecal culture (HEY media) and serum ELISA (IDEXX) from 8 Minnesota dairy herds over 9 years, and 970 fecal culture (TREK) from 3 Wisconsin dairy herds for 4 years were used to build a stochastic Markov Chain model for the within-herd spread of MAP and estimate its parameters. The infection/disease states were Susceptible, Latent, Low Shedder, Heavy Shedder and Clinical. Test parameters estimated with a latent-class Bayesian model were used to simulate a longitudinal disease trajectory for each tested animal. The uncertainty distributions of the IDM parameters were estimated iteratively using the animal-level trajectories. The parameter means were similar to those obtained using traditional MLE methods (at 95% confidence level) but the new method also produced joint uncertainty distributions unavailable elsewhere. Functional box-plots were used to validate the predicted animal trajectories via simulation studies.