Serological Diagnosis of Bovine Neosporosis: A Bayesian Evaluation of two Antibody ELISA Tests

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Introduction

Currently, there are no perfect reference tests for the in vivo detection of *Neospora caninum* infection in cattle. Two commercial ELISA tests for the detection of *N. caninum*-specific antibodies and currently used in Belgium for bovine sera: the *Neospora Caninum* Antibody Test Kit® from IDEXX [TEST A] and the Bio-X K218 Competition ELISA® from BIOX [TEST B].
The goal of this study was to evaluate these tests with a no gold standard approach, for the test purpose of: (1) demonstration of freedom of infection at purchase, and (2) diagnosis in aborting cattle.

Materials and Methods

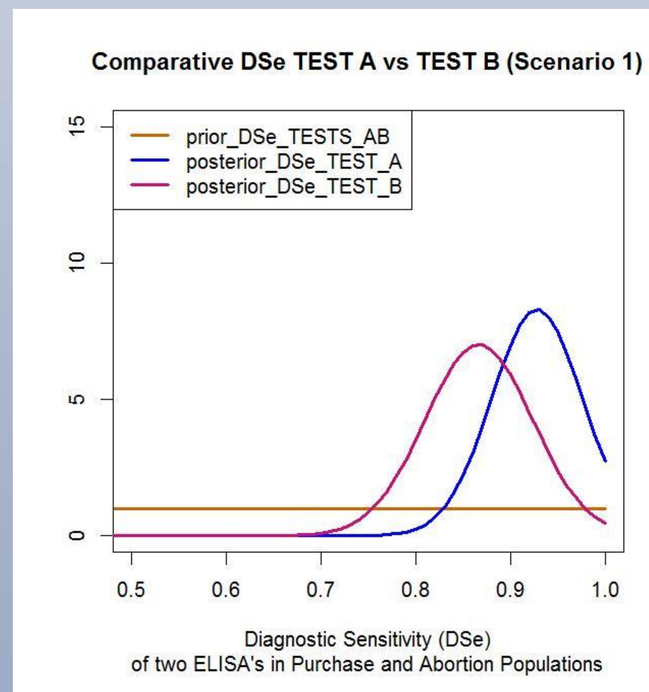
Sera of two study populations, Abortion (AB; n=196) and Purchase (PUR; n=514), were selected and tested with both ELISA's. Test results were entered in a Bayesian model with informative priors on population prevalence parameters only (Scen 1. = POP). The model was run in Winbugs and adapted from Dendukuri and Joseph (2001) and Branscum et al. (2005) for 2 tests in 2 populations with 2 Markov chains, including conditional dependence. As sensitivity analysis, two more model scenarios were used: one with informative priors on test diagnostic accuracy parameters (Scen 2 = TEST) and one with all priors uninformative (Scen. 3 = UN).

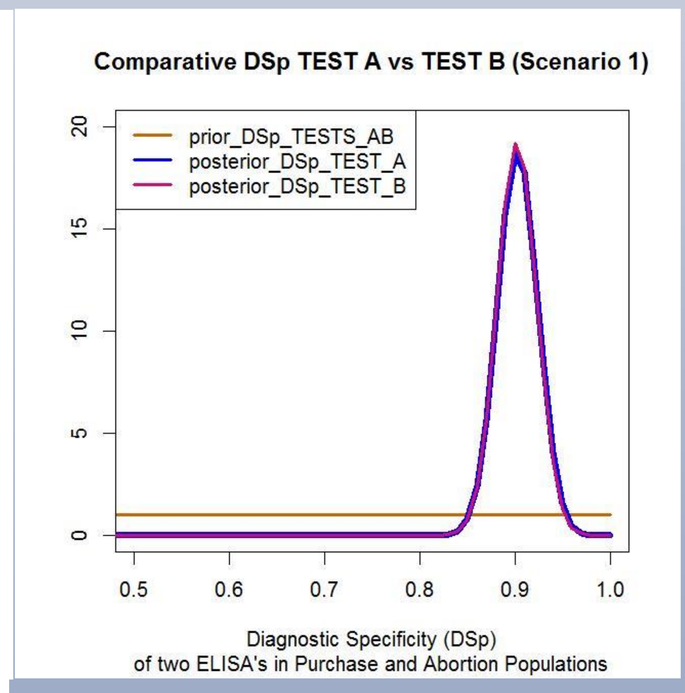
Results

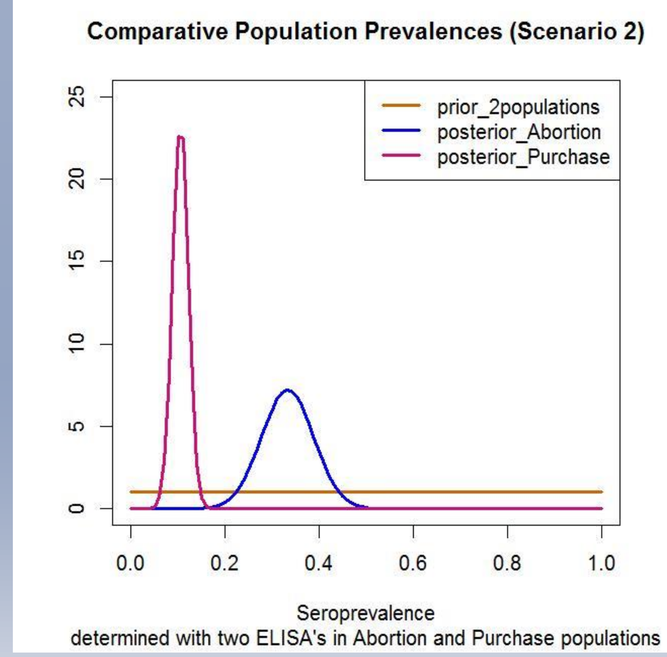
The accuracy parameters were estimated from the POP-model: diagnostic sensitivity (IDEXX: 93.54% - BIOX: 86.99%) and specificity (IDEXX: 90.22% - BIOX: 90.15%) were high and comparable (Bayesian p-values >0.05). Based on predictive values in the study populations, both tests were fit for purpose, despite an expected false negative fraction of +/-0.5% in PUR and +/-5% in AB population. In addition, a false positive fraction of +/-60% in PUR and +/-20% in AB population was found.

MODEL	Informative Prevalence (Scen.1) or Test priors (Scen. 2)		
PARAMETER	Prior Scenario	Median	95% Credibility Interval
DSe_TEST_A	Scen. 1	93.54%	81.74 - 99.56%
DSe_TEST_B		86.99%	74.78 - 97.05%
DSp_ TEST_A		90.22%	86.31 - 94.64%
DSp_ TEST_B		90.15%	86.31 - 94.52%
Prevalence_Abortion	Scen. 2	44.02%	36.50 - 51.50%
Prevalence_Purchase		10.46%	7.22 - 13.90%
Covariance_Infected	Scen. 1	0.0089	-0.0082 - 0.0741
Covariance_Non-infected		0.0726	0.0372 - 0.1013
Correlation_Infected		0.1407	-0.0864 - 0.5981
Correlation_Non-infected		0.8229	0.6619 - 0.9211
NPV_TEST_ A_Purchase		99.69%	98.89 - 99.98%
NPV_TEST_B_Purchase		99.38%	98.40 - 99.88%
PPV_TEST_ A_Purchase		29.71%	12.46 - 59.23%
PPV_ TEST_B_Purchase		28.06%	11.66 - 57.10%
NPV_ TEST_ A_Abortion		97.06%	91.52 - 99.83%
NPV_ TEST_ B_Abortion		94.27%	88.75 - 98.85%
PPV_ TEST_ A_Abortion		79.94%	70.54 - 89.40%
PPV_ TEST_ B_Abortion		78.69%	68.72 - 88.46%

Table: Posterior estimates from the Bayesian Simulations, using two informative prior scenarios.; TEST A: IDEXX - TEST B: BIOX; DSe: diagnostic sensitivity; DSp: diagnostic specificity; NPV: test negative predictive value; PPV: positive predictive value







Figures: Comparison of the posterior distributions of:
- Test* diagnostic sensitivities (DSe)
- Test *diagnostic specificities (DSp)
- Population prevalence in the Abortion and Purchase populations

* TEST A: IDEXX - TEST B: BIOX

Discussion

Since no perfect reference tests are available for in vivo detection of *Neospora caninum* infection in cattle, this no gold standard Bayesian comparative study demonstrated that in the Belgian setting both tests under evaluation obtained comparably high accuracy, similar to what is claimed by the producers or described in literature. The observed differences were not significant, as demonstrated by the large overlap in posterior distributions and by Bayesian p-values >0.05.
Based on predictive values in the study populations, both tests are indeed largely "fit for purpose" for the two designated purposes: (1) purchase examination [freedom], (2) abortion screening [diagnosis], despite the expected false negative (+/-0.5% in PUR; +/-5% in AB) and false positive (+/- 60% in PUR; +/-20% in AB) fractions.
Clinicians and laboratories need to take these test characteristics into account when using them in the individual diagnostic process, and may consider confirmation testing, especially for seropositive results.

References : Dendukuri N. & Joseph L., 2001. Bayesian approaches to modeling the conditional dependence between multiple diagnostic tests. Biometrics 57, 158-167 ; Branscum A.J., Gardner I.A. & Johnson W.O., 2005. Estimation of diagnostic-test sensitivity and specificity through Bayesian modeling. Prev.Vet.Med. 68, 145-163.

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