Bayesian evaluation of diagnostic accuracy of two commercial Leptospira Hardjo antibody ELISA's in bovine sera.

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Introduction

In Belgian cattle, epidemiological information on L. Hardjo (LH) seroprevalence is missing and diagnosis of leptospirosis remains challenging. A previous gold-standard comparison to an LH-specific microscopic agglutination test (MAT) of two commercial diagnostic ELISA's: Linnodee® and Prionics, indicated higher agreement (kappa) for Prionics®. However, MAT is not a perfect gold standard: diagnostic performance may depend on stage of illness (acute ↔ convalescent). Therefore, a no-gold-standard Bayesian evaluation was performed to re-evaluate the diagnostic accuracy of these tests.

Materials and Methods

Two bovine study populations were selected: an **abortion population** (n=303, prevalence estimated 30%) was tested with all 3 tests and a **general population** (n=1831, prevalence estimated 1%) with the ELISA's only. The test results were cross-classified with non-interpretable results (NI) alternatively coded as negative, positive or excluded. A Bayesian model was adapted to account for conditional (in)dependence of test results. Prior information was collected to construct several prior-model-data scenarios and a sensitivity analysis led to a final set of simulations and data-driven results.

Results

The posterior estimates of DSe varied between 85-97%, with slight advantage for DSe Linnodee®. The 3 DSe medians were not significantly different and the MAT was indeed found to be imperfect. DSp estimates varied between 80-98% and consistently showed MAT and Prionics® medians as slightly higher compared to Linnodee®, the difference often being statistically significant. The results compared well to the previous gold-standard analysis of the same data.
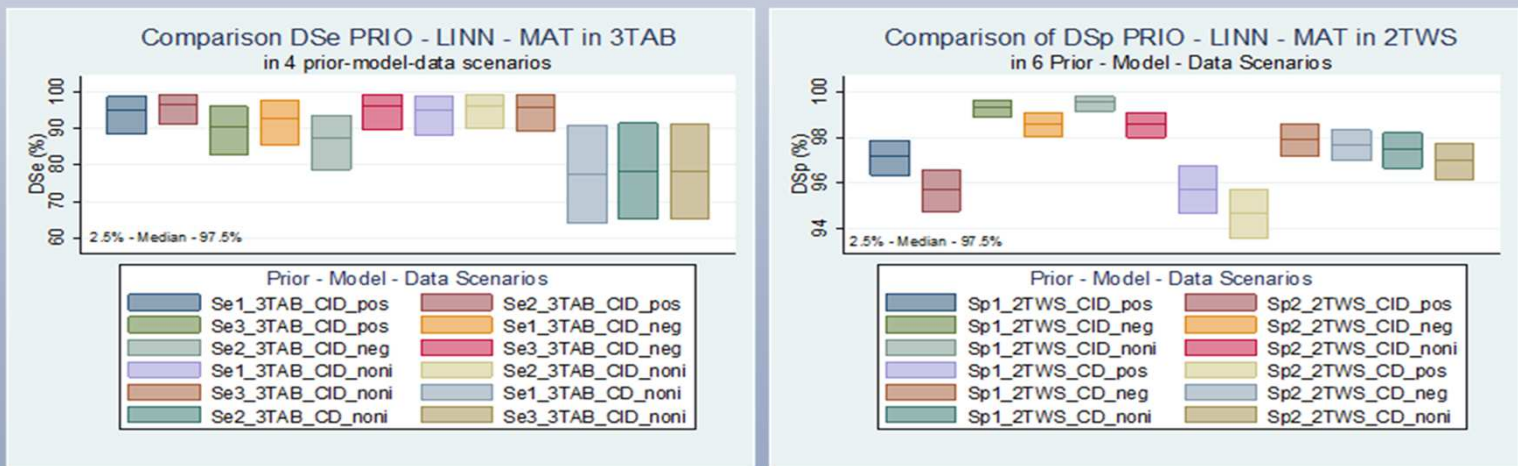
Discussion

Advice was given to interpret these results from multiple simulations according to the test's **intended purpose.**

When tests are used to detect exposure to LH in **aborting or convalescent** cattle, one should ideally select the most sensitive test and interpret NI samples conservatively (as positive) to exclude false negatives. When performing **surveillance and controlling** for LH-exposure/infection in the general cattle population, one could select for more specificity with a progressive interpretation of NI samples (as negative) to exclude false positives. In the first case, both Linnodee® and Prionics® are considered equally valid choices, in the second case there is a slight advantage for the Prionics® ELISA.

Abortion : Linnodee ~ Prionics				Surveillance : Prionics > Linnodee			
Parameter	CrI: 2.5%	Median	CrI: 97.5%	Parameter	CrI: 2.5%	Median	CrI: 97.5%
Se PRIO	88.39%	94.96%	98.84%	Sp PRIO	98.86%	99.32%	99.66%
Se LINN	91.19%	96.72%	99.33%	Sp LINN	98.03%	98.62%	99.08%

A larger sample size might still reveal significant differences in DSe, probably in the opposite direction as observed for DSp, with Linnodee® gaining advantage over Prionics®. Given that in certain screening situations (e.g. serial testing) false positives are not a major problem, the **test preference may potentially change** towards highest DSe. No account was taken of the animal's (unknown) vaccine status and since none of the tests are "DIVA", the seropositive LH-exposed group may include some vaccinated animals. None of the tests were suitable to obtain a causative diagnosis of leptospirosis or to give information on other Leptospira serogroups.