Evaluation using latent class models of the diagnostic performances of three ELISA tests commercialized for the serological diagnosis of Coxiella burnetii infection in domestic ruminants

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Thibaut Lurier[1, 2], Elodie Rousset[3], Patrick Gasqui[1], Carole Sala[4], Clément Claustre[1], David Abrial[1], Philippe Dufour[3], Renée de Crémoux[5], Kristel Gache[6], Marie Laure Delignette-Muller[7], Florence Ayral[2], Elsa Jourdain[1]

1- UMR EpiA; 2- USC 1233; 3- Q fever NRL; 4- EAS Unit ; 5- UMT PSR; 6- GDS France; 7- UMR 5558

Context and objectives

Context

- ELISA methods are recommended for the serological diagnosis of *Coxiella burnetii* infection in ruminants
- Without Gold Standard, accurate estimates of their Sensitivity (Se) and Specificity (Sp) are lacking

Objectives

- Assess Se and Sp of the ELISA tests available in France in sheep, goats and cattle
- Estimate optimal sample sizes considering sensitivity and specificity at herd level

Name used in the current study	Test 1	Test 2	Test 3
Commercial name	IDEXX Q fever Ab test	PrioCHECK™ Ruminant Q Fever	ID.Vet ID Screen® Q fever indirect multi-species
Manufacturer	IDEXX	ThermoFisher Scientific	Innovative Diagnostics
Strain used for antigen production	Isolated from ticks (Nine Mile reference strain)	Isolated from an ewe	Isolated from a cow
Conjugate	Secondary antibodies biding to ruminant IgG	G protein	G protein

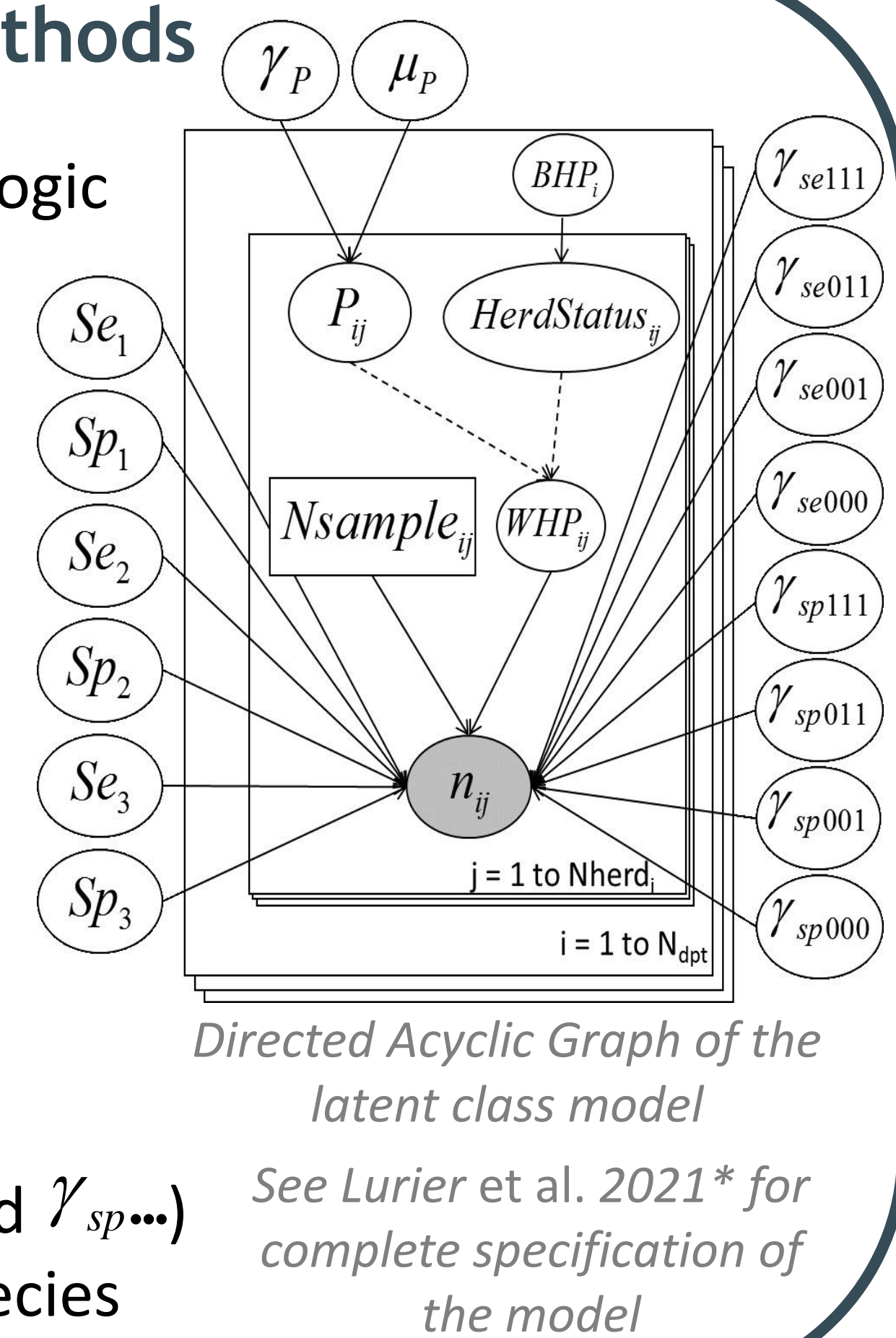*Characteristics of the three ELISA tests commercialized in France*

Material and methods

Data

- Sub-sample of a larger epidemiologic study (Gache *et al* 2017)
  1 413 **cows** from 106 herds
  1 474 **goats** from 103 herds
  1 432 **ewes** from 99 herds
- Serum collected and analyzed with the three ELISA tests at the NRL for Q fever

Latent class model

- Modeling of the cross-classified test results (n_{ij})
- Accounting for conditional dependence between tests ($\gamma_{se\cdots}$ and $\gamma_{sp\cdots}$)
- One model for each ruminant species

Directed Acyclic Graph of the latent class model

See Lurier et al. 2021* for complete specification of the model

Results at individual level

Se and Sp estimates

- **Low Se** especially in sheep
- **High Sp** but lower in cattle
- **Test 3** was the most sensitive in all species but also the least specific
- Tests were **not equivalent** for each ruminant species

Diagnostic accuracy of the three ELISA tests
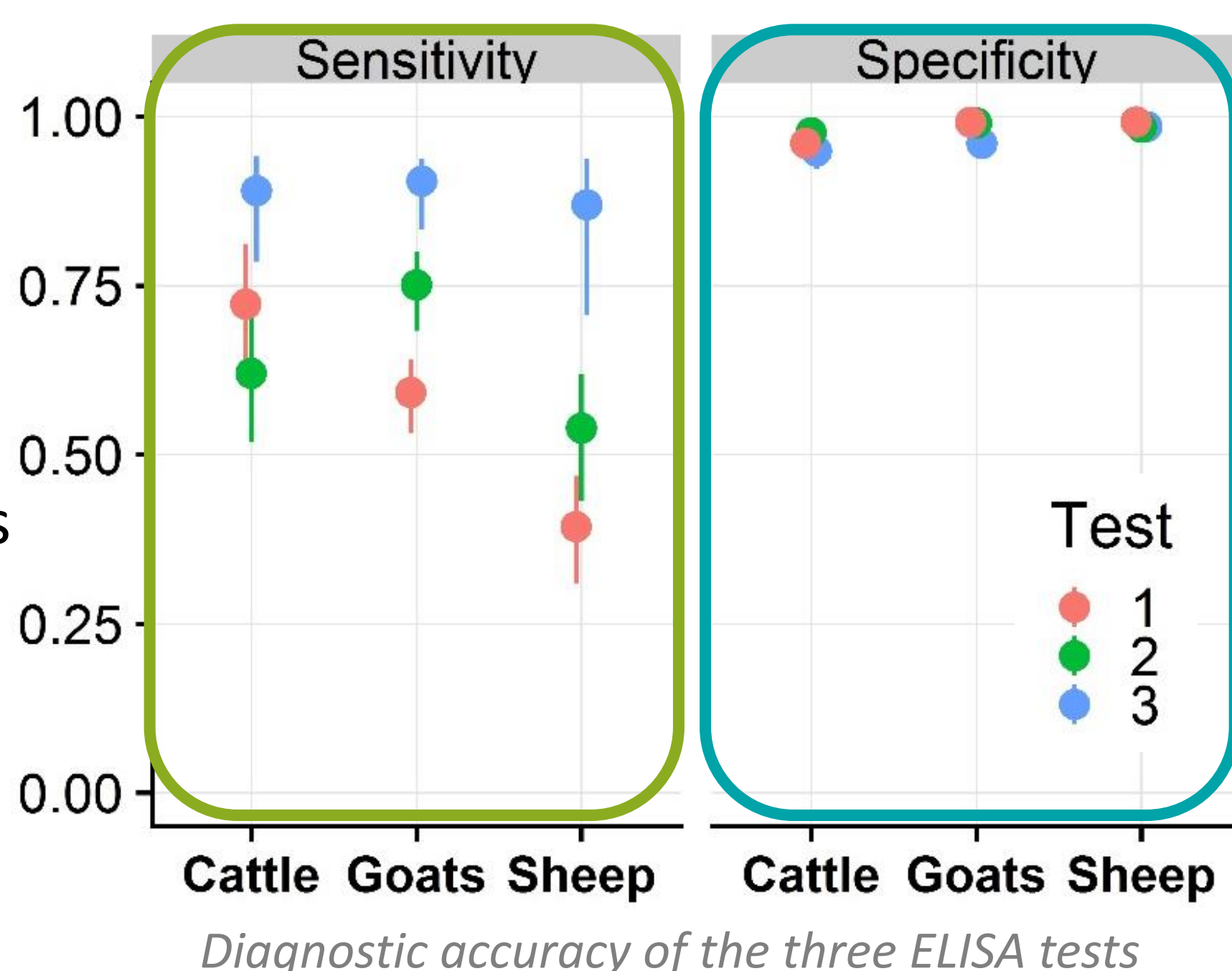
Conditional dependence (CD)

- **High CD between tests 1 and 2** in seropositive animals
⇒ Tests 1 and 2 tended to be **falsely negative at the same time**
- **Negligible CD** in seronegative **sheep** and **goats**
⇒ False positive results were **rare and independent** for the three tests
- **Low but positive** CD in seronegative **cattle** *
⇒ False positive results were **rare but dependent** in **cattle**

*Pairwise conditional dependence in truly seropositive (Se_T• T•) or seronegative (Sp_T• T•) animals*
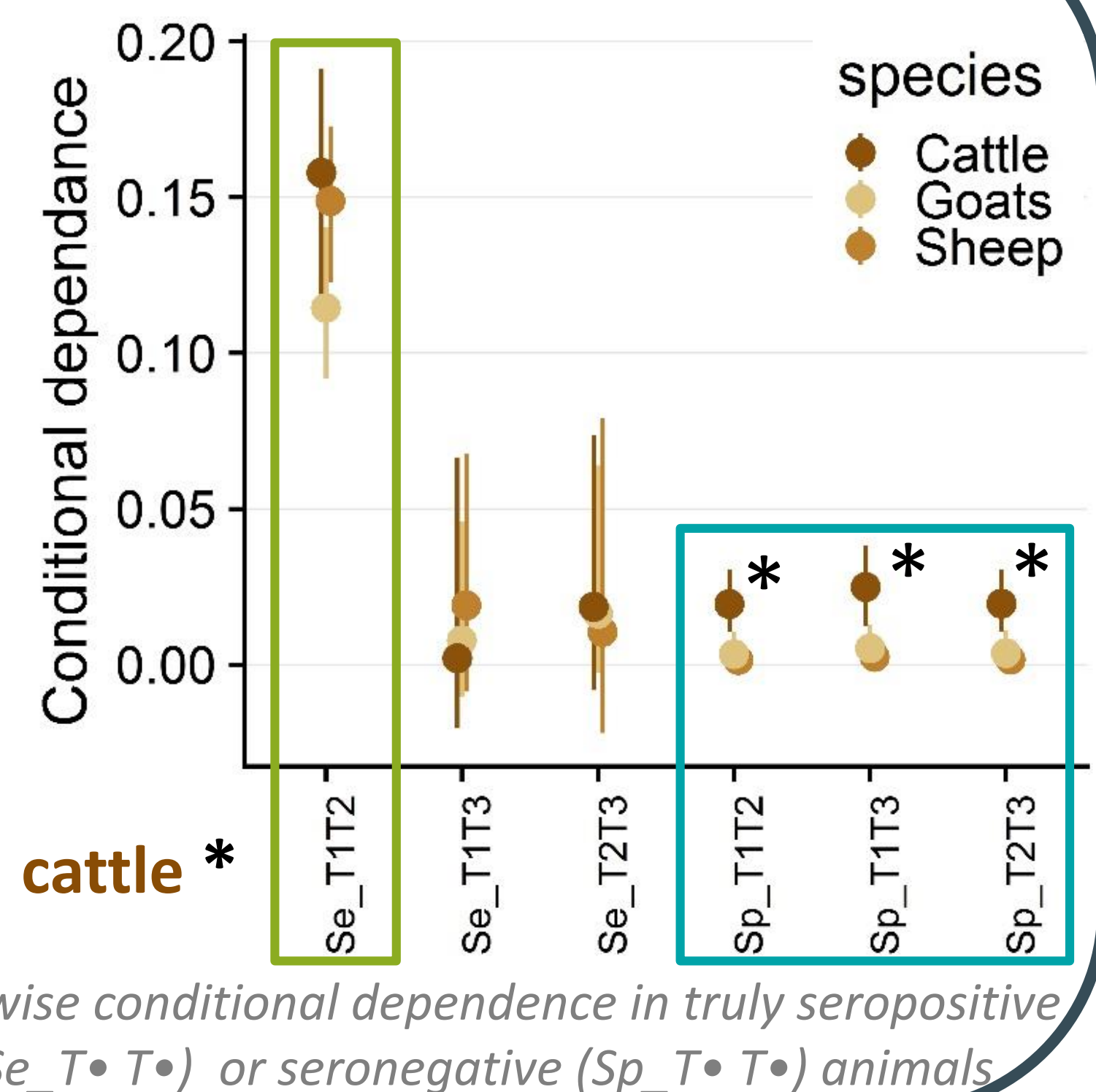
Results at herd level

Definitions

- **HSe** = *Probability that at least one animal sampled is positive using one test in a positive herd*
- **HSp** = *Probability that none of the animals sampled is positive using one test in a negative herd*
⇒ Calculated with a sample size varying from 1 to 20 animals

Results

- **HSe increased** with the sample size while **HSp decreased**
- **Test 3** had the worse HSp
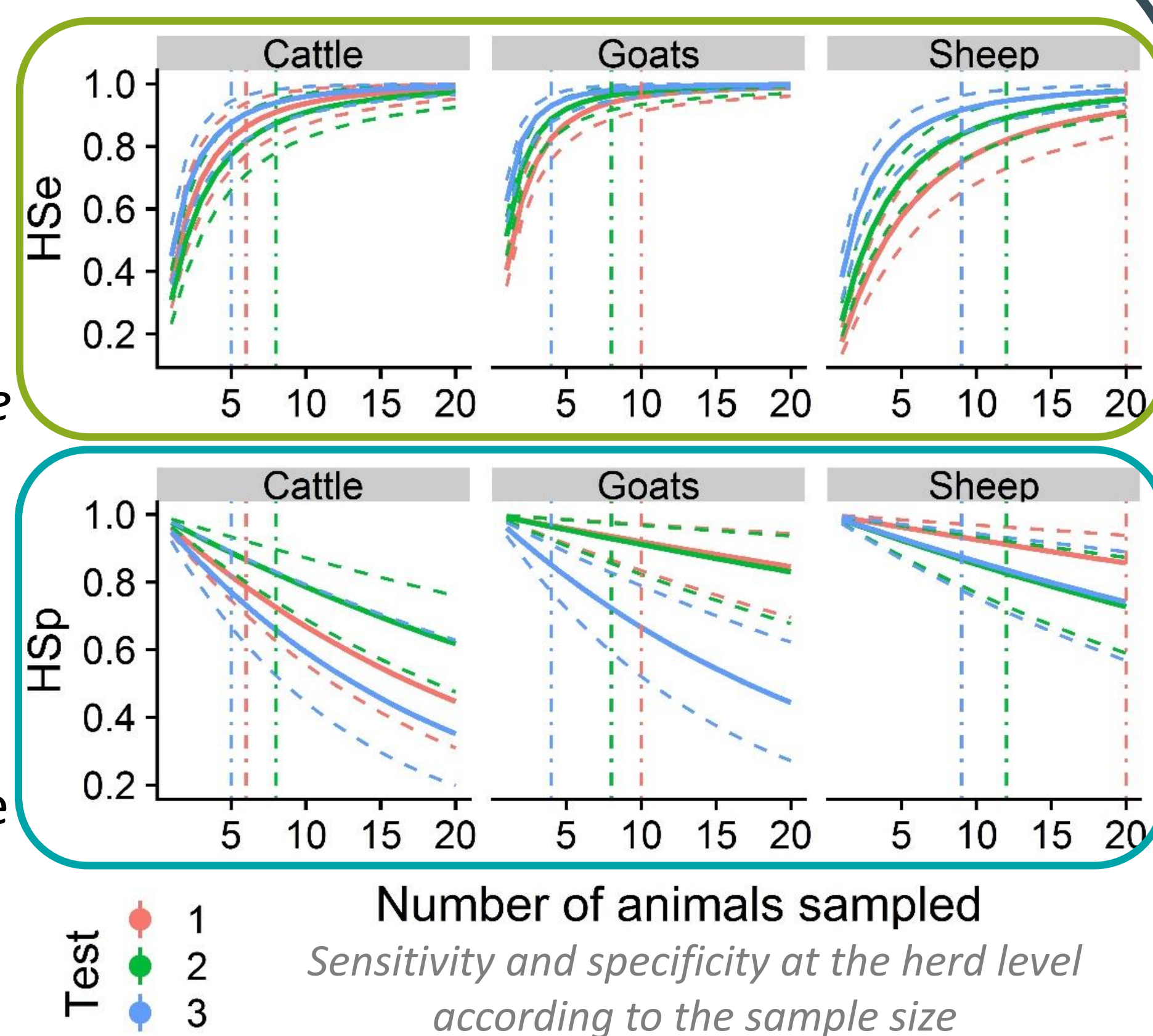
⇒ The **optimal sample size** maximizing both HSe and HSp **varied from 3 to at least 20** animals depending on the test and ruminant species

Sensitivity and specificity at the herd level according to the sample size

Discussion

- **Unbiased estimation** of Se and Sp without relying on an imperfect gold standard
- Compared to other studies : **similar Sp** but **lower Se**
⇒ Account for the high conditional dependence in seropositive animals between tests 1 and 2 (see poster #232)
- Applicability of Se and Sp estimated limited to a sero-epidemiological context (**different from herds with abortion** in which the test is often performed in practice)

Perspectives

- Account for the Se and Sp of the ELISA tests to **accurately assess the seroprevalences** of Q fever
- Need to reassess Se and Sp of the tests in an **abortive context**
- Discrepancies between tests and perspectives of application for an harmonization of the ELISA tests

* Lurier, T., Rousset, E., Gasqui, P., Sala, C., Claustre, C., Abrial, D., Dufour, P., de Crémoux, R., Gache, K., Delignette-Muller, M.L., Ayral, F., Jourdain, E., 2021. **Evaluation using latent class models of the diagnostic performances of three ELISA tests commercialized for the serological diagnosis of *Coxiella burnetii* infection in domestic ruminants.** Veterinary Research 52, 56. https://doi.org/10.1186/s13567-021-00926-w

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