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

ECBHM European College of Bovine Health Management

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INRAE la science pour la vie, l'humain, la terre

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VETERINARY RESEARCH

RESEARCH ARTICLE Open Access

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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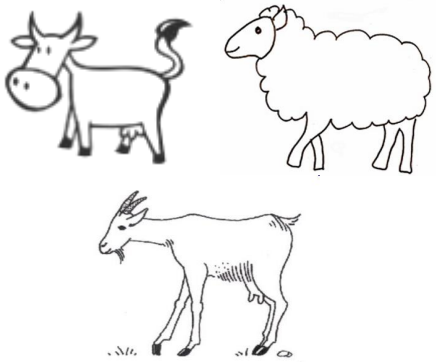
Q fever, a zoonotic disease transmitted by domestic ruminants

- Q fever is a zoonotic disease responsible for acute and persistent infection in humans
- Main Reservoir = Domestic ruminants : Reproductive issues
  - **1st infectious cause of abortion in Goat herds (27.3%)**
  - **2nd in Cattle (9.6%) and 3rd in Sheep (19%) herds**

(French Oscar network, 2022)



- Aim of the control of *Coxiella burnetii* in ruminants
  - **Public health** (zoonotic risk) and **economic** (reproductive issues)

⇒ **Mandatory surveillance** in Europe according to the new animal health law since 2021 (E category)

Diagnostic issues in domestic ruminants

- **Direct diagnostic :** Intermittent shedding in milk, vaginal secretions, feces

  ⇒ PCR : Sp = 100% but **low Se** except after abortion

- **Indirect diagnostic** : 3 ELISA tests commercialized in Europe

No Gold Standard test

- Diagnostic accuracy?
- Not assessed in every species
- Se considered to vary between 70 and 100%
- Sp considered to vary between 90 and 100%

⇒With some **methodological risk of bias**

- Comparison to **an imperfect reference test**
- No or inefficient modelling **of the conditional dependence between tests**

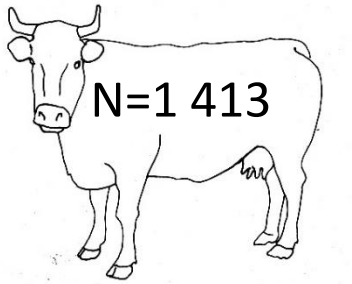
(Emery et al., 2012; Horigan et al., 2011; Lucchese et al., 2016; Muleme et al., 2016; Paul et al., 2013; Wood et al., 2019)

Objectives

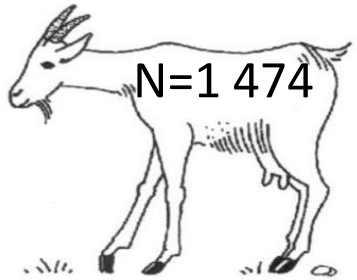
- To assess **Se and Sp** of the three commercialized ELISA tests for Q fever at the **individual level**
- To assess **Se and Sp** at the **herd level**
- To estimate the **optimal sample size for** detecting Q fever in a herd for each test in each species

Study sample

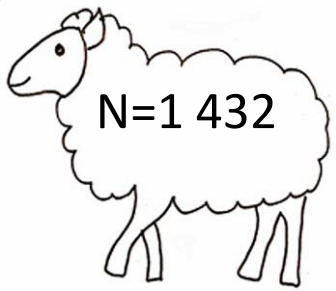
- Sub-sample of a larger epidemiologic study* of 23 000 animals sampled from 1500 randomly selected herds with no history of Q fever vaccination
- Inclusion of 150 animals from 10 herds in each *department*



106 Herds



103 Herds



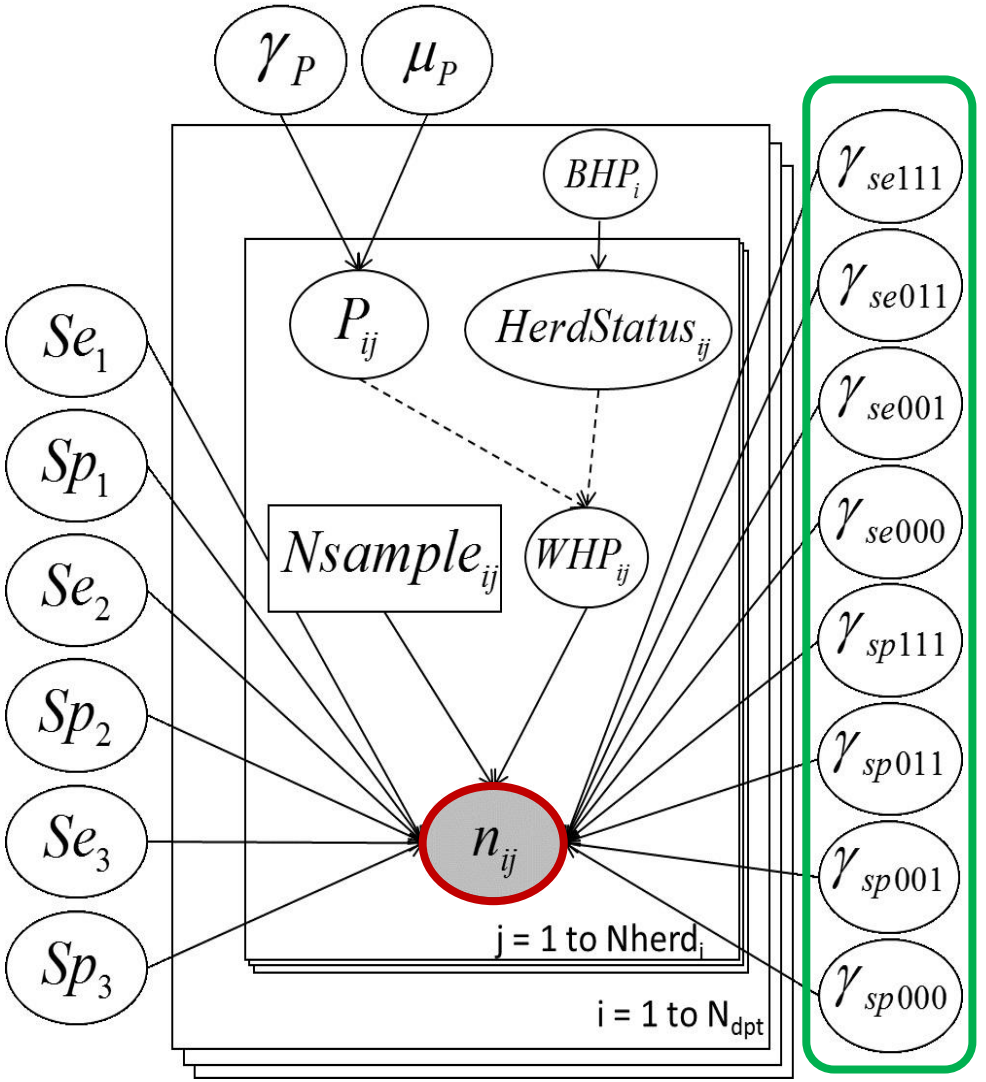
99 Herds

- Serum collected and analysed with the three ELISA tests at the NRL for Q fever in France

*(* Gache et al. 2017)*

Latent class model

- Modelling the **crossed-classified test results in each herd (n_{ij})**
- Accounting for **conditional dependence** between tests ($\gamma_{Sp...}$ and $\gamma_{Se...}$)
- One herd = one population
- A unique Between-Herd seroprevalence by department
  - With the possibility that some herds were **free of *C. burnetii*** seropositivity
- **Bayesian inference**
  - JAGS
  - Non informative prior distributions

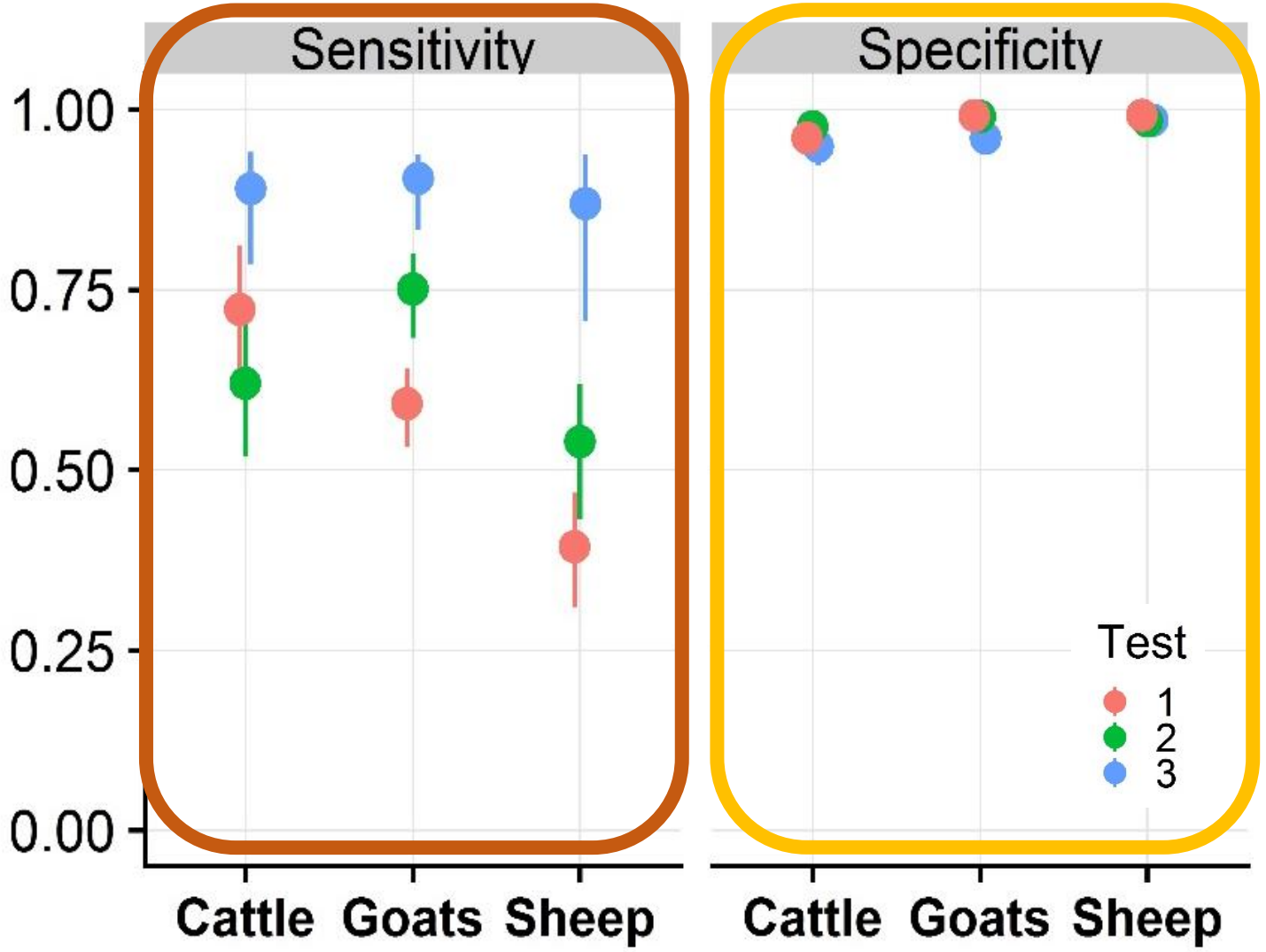


Results : Se and Sp estimates

- **Low Se** especially in sheep
- **High Sp** (slightly 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

⇒Which test use in each species?



Results : Conditional dependence (CD)

- **High CD between tests 1 and 2** in seropositive animals

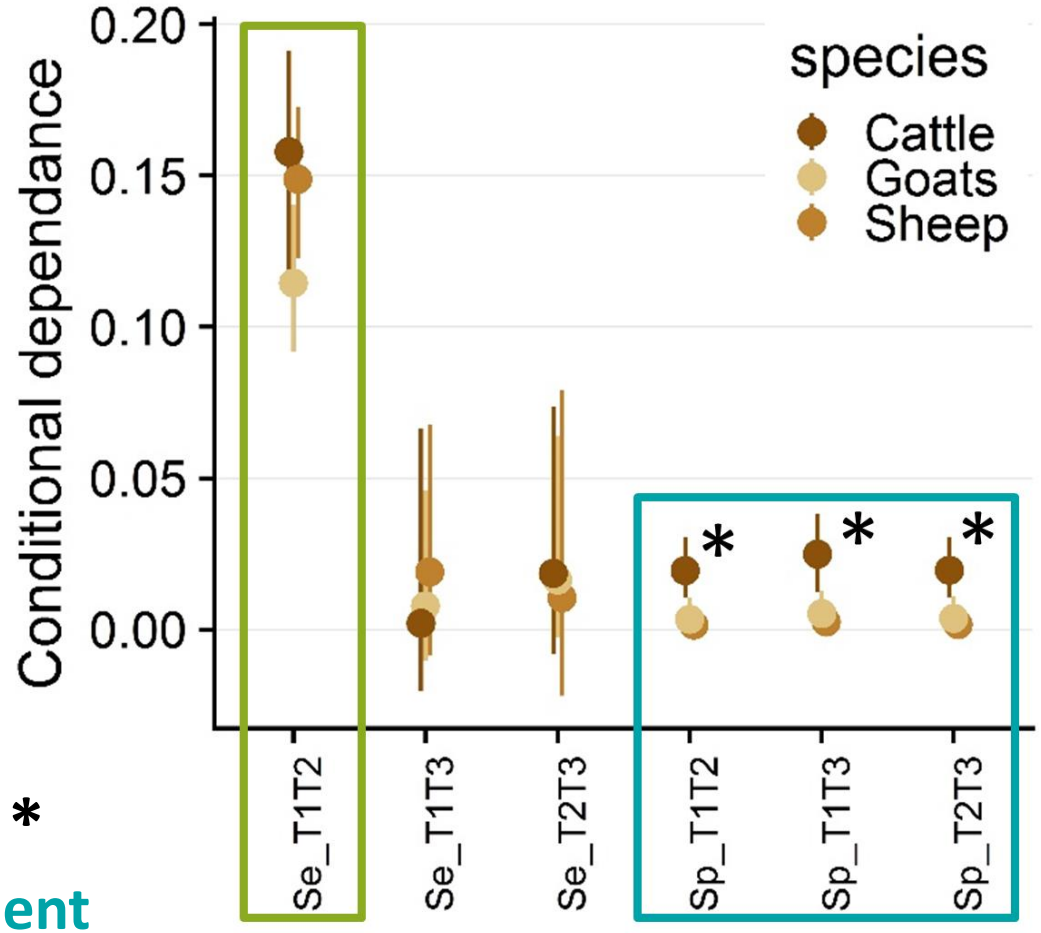
⇒ Tests 1 and 2 tended to be **falsely negative at the same time**

- **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**



At the herd level : Definitions

- **HSe** = *Probability that **at least one** animal sampled is positive using one test in a **truly seropositive herd***

- **HSp** = *Probability that **none** of the animals sampled is positive using one test in a **truly seronegative herd***

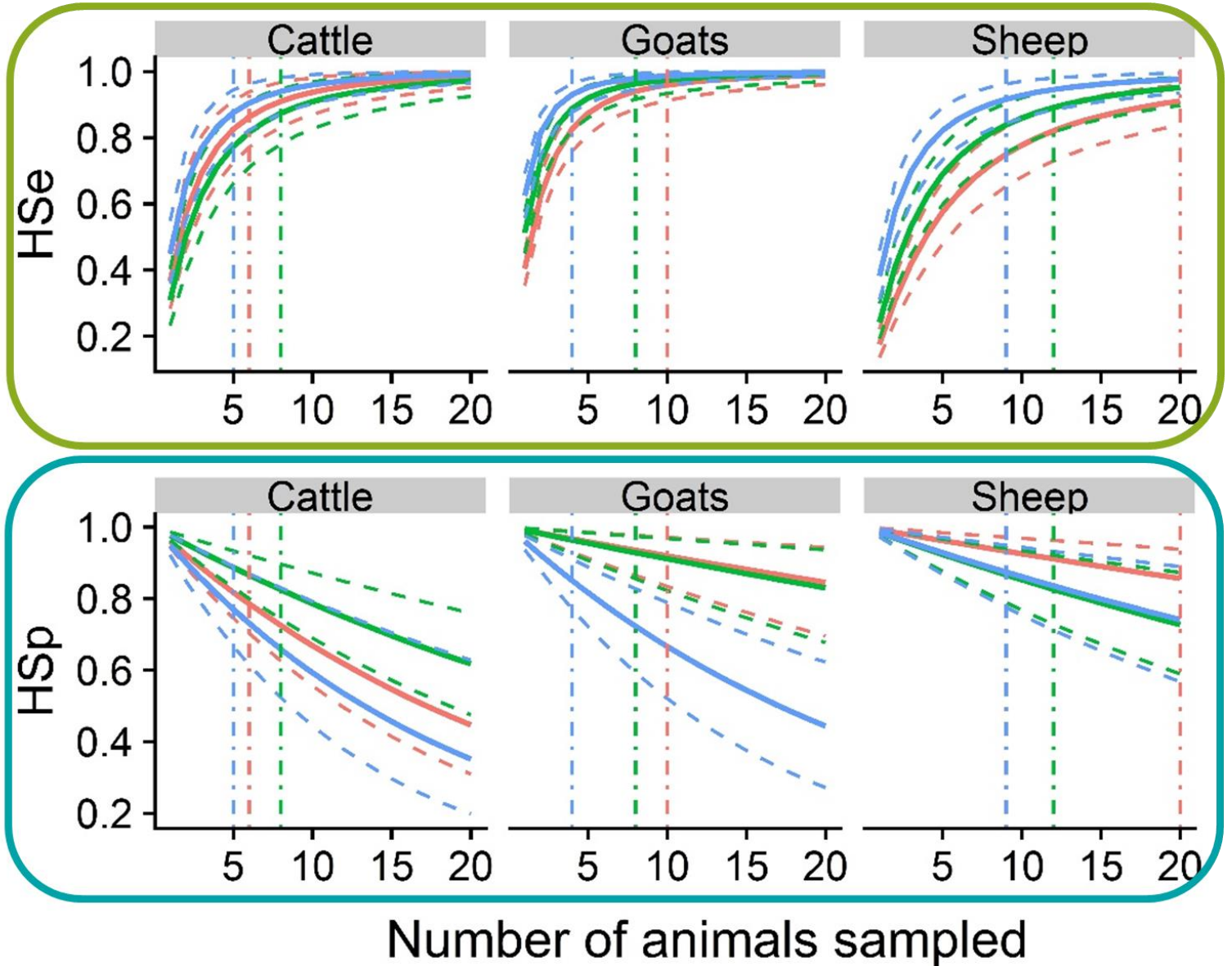
$\Rightarrow$ Calculated with a sample size varying from **1 to 20** animals

- « Optimal » sample size calculated to maximizing the **HSe** + **HSp**

At the herd level : Results

- **HSe increased** with the sample size while **HSp decreased**
- **Test 3** had the worst 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



Discussion : usefulness and validity of the model

- Unbiased estimation of Se and Sp
  - Did not rely on an imperfect Gold standard
  - Take into account the conditional dependence between tests
- Compared to other studies
  - Similar specificity
  - **Lower sensitivity**

  ⇒**Better modelling of conditional dependences in seropositive animals**
- High conditional dependence between tests 1 and 2
  - Only highly seropositive animals are positive with tests 1 and 2
  - Identification of all « seropositive » animals with test 3?
- **Optimal sample size to adapt according to species and tests**

Perspectives

- Necessity to account for ELISA tests Se and Sp to **accurately assess Q fever seroprevalences**
- Need to also assess the respective Se and Sp of the tests corresponding to **abortive contexts**
- Perspectives of harmonization of the 3 tests by changing positivity thresholds

Thank you for your attention

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  - VetAgro Sup
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  - The veterinarians who collected the samples
  - The Departmental Veterinary laboratories that performed the analyses
  - Animal Health Farmers' Organizations that coordinated the study locally

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