ELISA AND FAECAL CULTURE FOR DIAGNOSIS OF CAPRINE PARATUBERCULOSIS: SENSITIVITY AND SPECIFICITY OF EACH METHOD

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ABSTRACT : Two latent class models [maximum likelihood (ML) methods and Bayesian inference (BI)] were used to estimate the sensitivity (Se) and the specificity (Sp) of a serum ELISA (commercial Kit) and a faecal culture for the detection of infection with Map in French dairy goats. Samples of blood and faeces were collected in 532 goats from 15 herds.
Estimates according to ML and BI methods were different. Based on their precision, Bayesian inference was considered as the best method. Furthermore, BI gave true probability intervals and allowed the use of well-documented prior information, which summarizes expert opinion.

OBJECTIVES

Alternatively to previous methods referring to histo-pathological assays of *Mycobacterium avium paratuberculosis* (Map) infection in goat, to estimate the diagnostic sensitivity (Se) and specificity (Sp) of the ELISA and of faecal culture (FC) by 2 latent class models (maximum likelihood method and Bayesian inference) in two populations of dairy goats.

MATERIALS AND METHODS

1 – Samples
- Blood and faeces from 532 French dairy goats of different breeds and ages
- 15 herds in 2 sub-populations : herds without clinical signs vs with clinical signs, supposed to have different prevalences of Map infection.

2 – Testing
Serum tested with ELISA test kit according to manufacturer's recommendations (Inst. Pourquier, Montpellier, France).
Faecal culture on Herrold's Egg Yolk Medium (HEYM) following the French normalised text NF U47-103.
Tests were considered to be conditionally independent to each other (different biological bases: antibody vs antigen) and Se and Sp were supposed to be constant.

3 – Analysis
Latent-class models were used to estimate the Se and Sp of the ELISA and the FC (Se_{ELISA}, Sp_{ELISA}, Se_{FC}, Sp_{FC}): Maximum likelihood was estimated by the "TAGS" programme (Pouillot *et al.,* 2002) and Bayesian analysis was conducted by the freeware software WinBUGS (Branscum *et al*., 2005).
For Bayesian approach, prior information about the parameter is needed to obtain the posterior distribution of this parameter. Data obtained from Bayesian estimation in Greek dairy goats (Kostoulas *et al*., 2006) has been used for this purpose. Then, the mean or median of this posterior distribution can be used as an estimate of the parameter. A sensitivity analysis was then conducted by using relatively non-informative (NI) priors (Enøe *et al*., 2000).

RESULTS

Table 1 shows the cross-tabulation for the results of the two tests in the two populations and table 2 displays the estimations obtained under the different models.

Table 1: Cross-tabulation of the ELISA and FC results in the 2 sub-populations

Population 1	FC + (n)	FC – (n)	Total (n)	**Population 2**	FC + (n)	FC – (n)	Total (n)
ELISA +	2	1	3	ELISA +	13	13	26
ELISA -	6	311	317	ELISA -	15	171	186
Total	8	312	320	Total	28	184	212

Table 2: Estimations of Se,Sp and prevalence for the ELISA and the FC

Parameter	**ML model (%)** median (95% CI)	**Bayesian model (%)** median (95% PI)	**Bayesian model + NI (%)** median (95% PI)
Se_{ELISA}	51 (31-72)	61 (43-79)	53 (33-78)
Sp_{ELISA}	100 (NaN-100)	98 (97-99)	100 (98-100)
Se_{FC}	52 (34-69)	27 (18-37)	53 (34-72)
Sp_{FC}	99 (95 -100)	97 (95-98)	98 (96-100)
P_1	2 (0.5-6)	1 (0-3)	1 (0-4)
P_2	24 (16-34)	16 (11-23)	23 (14-34)

Se: Sensitivity, Sp: Specificity, FC: Faecal culture CI: Confidence interval, PI: probability interval , P1:prevalence in population 1 , P2: prevalence in population 2

DISCUSSION AND CONCLUSION

Compared to frequentist methods, the latent class model methods give estimates referring to the (latent) true disease status. Thus, these methods are specifically useful for a chronic disease like paratuberculosis (Branscum *et al*., 2005).
Result confirms that the prevalences were different in the 2 populations, which was a condition required for using these methods. The estimates of Se for ELISA and faecal culture according to the Bayesian model appeared to be different from estimates by the ML model or by the Bayesian model with non-informative (NI) priors whereas the estimates of these 2 lasts models (ML and BI+NI) are very close. The precision of estimates by BI (with informative prior) was better than with the 2 others models as the standard deviation (S.D.) of its marginal posterior distribution is smaller.
Compared to the ML approach, BI provides point estimates and intervals without the necessity of a large sample size and give true probability intervals. BI allows also the use of well-documented prior information, which summarizes expert opinion. Therefore the question of the priors is a point of great importance. They would ideally be based on previous studies that are similar to the current one (Enøe *et al*., 2000).
The better estimations of the accuracy of the 2 tests are obtained by the WinBUGS model with informative priors. Estimations are similar with the results of Greek dairy goats (obtained with another ELISA test), except for the Se_{FC} which is higher.

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