Bayesian estimation of accuracy and misclassification cost terms of ELISA on bovine bulk tank milk for predicting herd status for *Salmonella* Dublin

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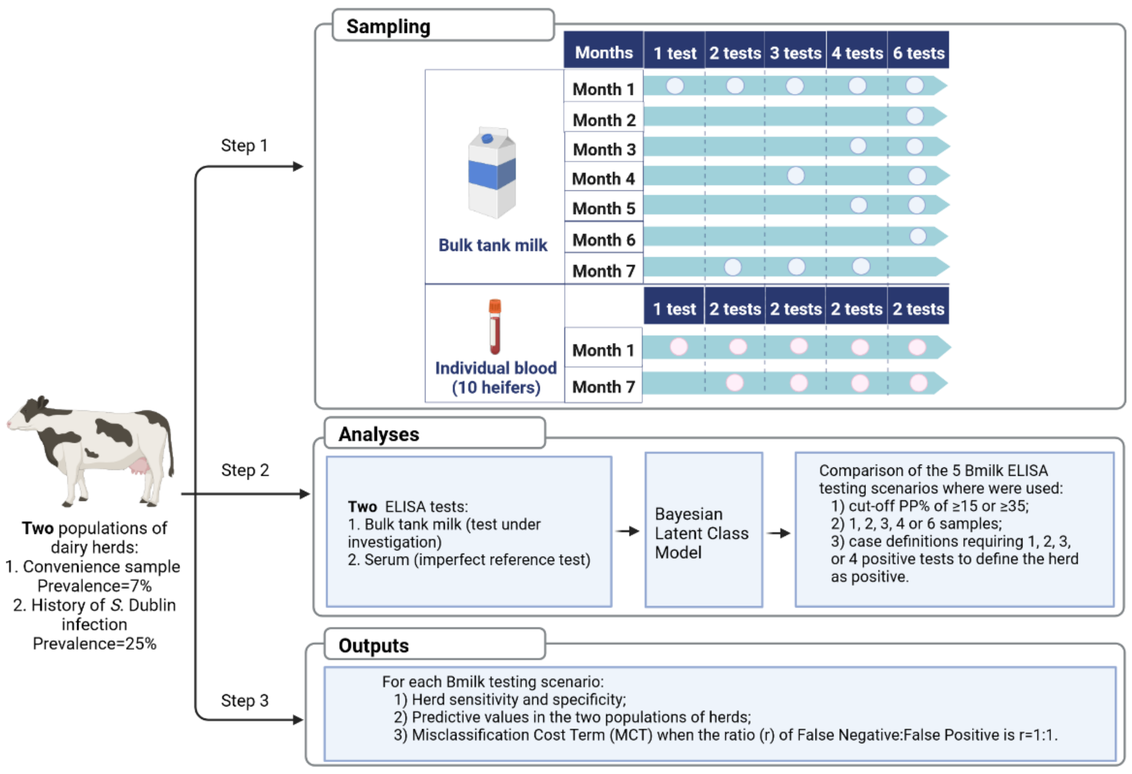
Introduction

- ***Salmonella* Dublin** (*S*. Dublin) infection emerged in **dairy cattle** and humans in 2011 in Québec province, Canada (MAPAQ, 2015). The infection leads to economic losses associated with decreased milk yield, sudden dead in youngstock, abortion in adults, and decreased income from sold or culled animals.
- Currently, there is **no perfect test** to determine the herd-level status for *S*. Dublin.
- Our recent studies showed that *S*. Dublin **milk ELISA** used on a single **bulk tank milk** sample is a convenient diagnostic test for classifying truly negative herds using the cut-off PP% ≥ 15 (Um et al., 2020; Um et al., 2022).
- In Québec's context (low prevalence of *S*. Dublin), herds assigned a *S*. Dublin negative status based on a test-negative bulk tank milk have high probabilities to be true negatives; negative predictive value was 95.8% (92.1-99.2) at cut-off PP% ≥ 15.
- However, herds testing positive on **one single** bulk milk ELISA test should seek a **confirmation** of this status with **complementary diagnostic methods**, since most of them will be false-positive results; positive predictive value was 26.6% (8.8-60.2) at cut-off PP% ≥ 15.

Objectives

Therefore, our objectives were to evaluate: (i) the **accuracy** of **different testing scenarios** using repeated antibodies measurement (ELISA) on bulk tank milk, and (ii) the **misclassification cost terms** in two populations of herds with known prevalences of *S*. Dublin.

Materials and methods



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Results

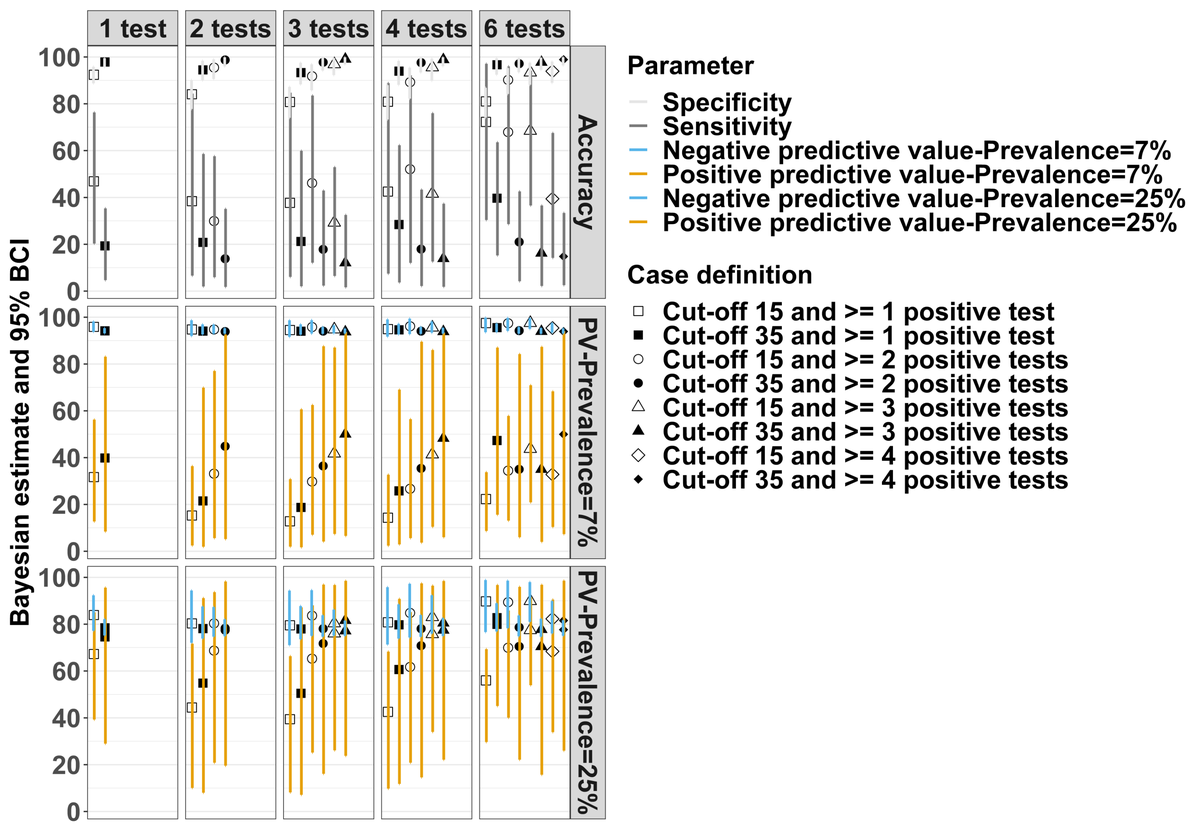

Figure 1. **Accuracy** at herd-level (sensitivity and specificity) and predictive values (PV) of **bulk milk (Bmilk) ELISA** for five testing scenarios (1, 2, 3, 4, 6 tests) and 8 interpretations to define a herd as positive (case definition) in 2 populations of herds (prevalence=7% and 25%).

(i) Testing **more than one Bmilk** (i.e. 2 to 6 tests) had a **little increasing effect** on the specificity of Bmilk ELISA. Notably, when the **strictest** case definition was used to conclude on *S*. Dublin positive status. Then, when applied in the two populations, the same pattern was observed for **positive predictive values**, however estimated with less precision.

(ii) Among all the testing scenarios, testing **3 Bmilk** using Bmilk ELISA **cut-off PP% ≥ 35** and **requiring 3 positive results** led to the **highest specificity**; specificity was **99.1% (96.8-99.9)**.

(iii) Testing a **single Bmilk** and using the **most liberal** case definition led to **better sensitivity** estimates, except for 6 Bmilk, which led to sensitivity of 72.3% (30.3-97.1). The **negative predictive values** followed the same pattern and remained high (median estimates of 93.7% to 97.5% and 77.2% to 89.8% in the 7%- and 25%-prevalence population, respectively).

Results (continued)

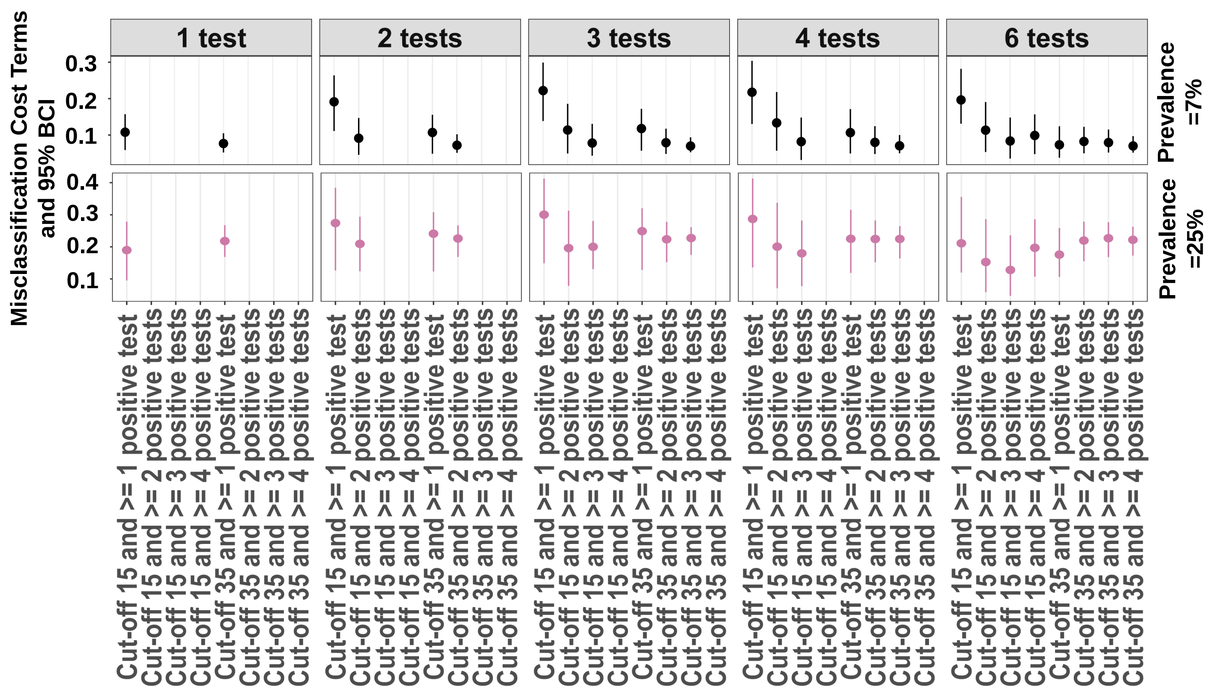

Figure 2. **Misclassification Cost Terms** (MCTs) of **bulk milk (Bmilk) ELISA** for five testing using a False Negative : False positive ratio of 1:1 in the two populations of herds (prevalence=7% and 25%).

(i) In the population of herds with prevalence of 7%, testing **more than one Bmilk** at **cut-off PP% ≥35** and **requiring** the **maximum** number of **positive results** to conclude to positivity led to **the best MCT** estimates (i.e. the lowest misclassification costs); the median values ranged from 0.070-0.072.

(ii) While, in the population of herds with prevalence of 25%, testing **6 Bmilk** at **cut-off PP% ≥15** and requiring **3 positive results** led to the **best MCT** estimate (0.128; 0.047-0.236).

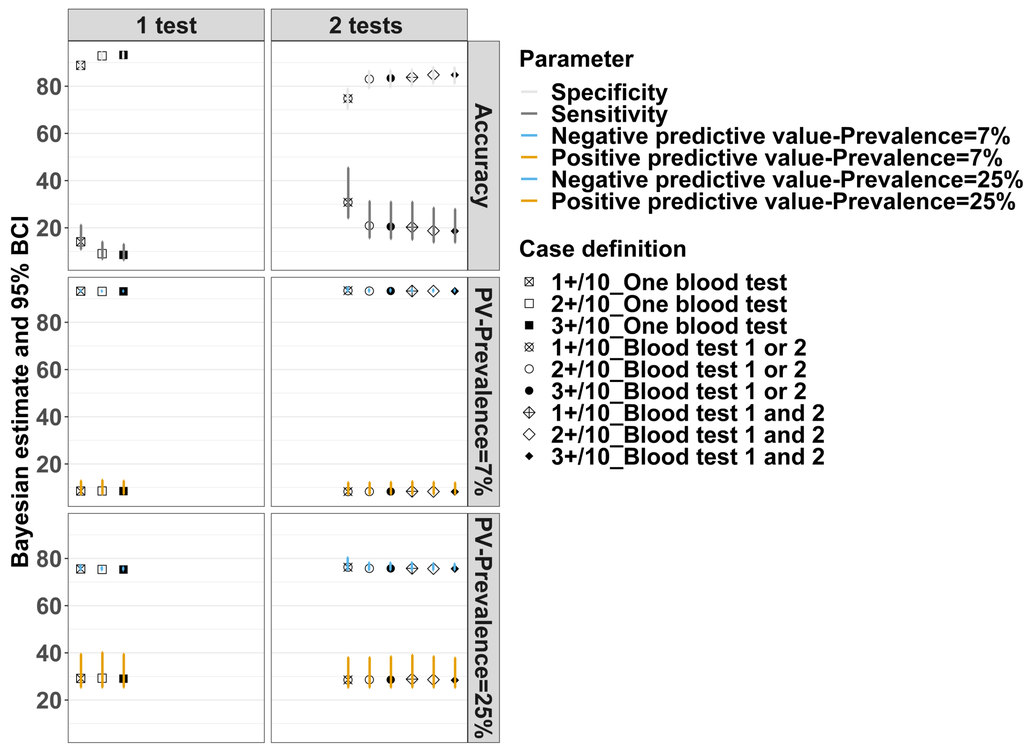

Figure 3. **Accuracy** at herd-level (sensitivity and specificity) and predictive values (PV) of **serum ELISA** performed on 10 individual sera (1 test) and 20 individual sera (2 tests) and 9 interpretations to define a herd as positive (case definition) in the two populations of herds (prevalence=7% and 25%).

(i) Performing a **single blood test** on 10 individuals (i.e. **10 sera**) led to **better serum ELISA specificity** compared to 2 tests, regardless of the case definition.

(ii) Performing **two blood tests** (i.e. **20 sera**) led to **better serum ELISA sensitivity** vs. 1 test. Notably, when the **most liberal** case definition was used (i.e. 1+/10 at test 1 or 2).

(iii) When applied in the two populations, there was almost **no effect of testing 20 sera** neither on the positive nor on the negative predictive values compared to only 10 sera, regardless of the case definition.

Conclusions and benefits

- The consideration of both the **accuracy** of milk ELISA test used on multiple bulk tank milk samples and **misclassification cost terms** highlighted that the selection of the optimal testing scenario **depended on the producer priority** (the importance given to false negative vs. false positive test results) and the **disease history** of the herd.
- Nevertheless, approaches based on **as few as two Bmilk** could be recommended to identify uninfected herds with high certainty.

Perspectives

- The dairy producers and veterinarians could develop a testing strategy (i.e. biological sample, number of samplings, diagnostic test, and case definition to define a herd as positive) according to their primary objective.
- The next step of our study is to use the **Multiple Criteria Decision Analysis** (MCDA), which is an interesting approach for providing a decision support tool to select testing scenarios and cut-offs in our local epidemiologic context.

References

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