



Using Gaussian Finite Mixture Models To Estimate The Lymphocyte Count Reference Interval In Normal Dairy Cows And The Most Discriminant Threshold To Identify Cows With Bovine Leukosis.

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INTRODUCTION

Lymphocyte count in cattle

- ❖ Differs between normal and leukosis-positive cows. Leukosis often leads to elevated blood lymphocytes count (LC), or, toward the end of the disease, to lymphopenia.
- ❖ Lymphocyte count is also known to vary with age in normal cows, with slightly higher LC in younger cows.

GFMM

- ❖ Gaussian finite mixture model (GFMM) is an unsupervised machine learning approach that can be used to find the most probable normal distributions (generally two) that could explain the overall distribution of a given biological parameter.

Obj. 1

- ❖ Describe, using GFMM, the LC distributions in normal vs. leukosis-positive cows

Obj. 2

- ❖ Assess whether LC distributions differs between cows aged 2 to 4 year. vs. cows ≥ 4 year old.

METHODOLOGY

Prospective observational study (2023; QC, Canada):

- ✓ 8 dairy farms (prevalence of leukosis varying from 3% to 90%).
- ✓ Hematological results available for 632 cows.

Data analyses:

❖ Bayesian Gaussian finite mixture model (GFMM):

- ✓ Describe the two most probable Gaussian distributions within the overall LC distribution.
- ✓ Accuracy estimates computed as described by Yang et al (2022).
- ✓ Youden index was used to identify the most discriminant LC threshold.



```
model_GFMM <- paste0("model{
  for (i in 1:num_obs){
    lymph_ct[i] ~ dnorm(mu[I[i]], prec[I[i]])
    I[i] ~ dcat(alpha)
  }

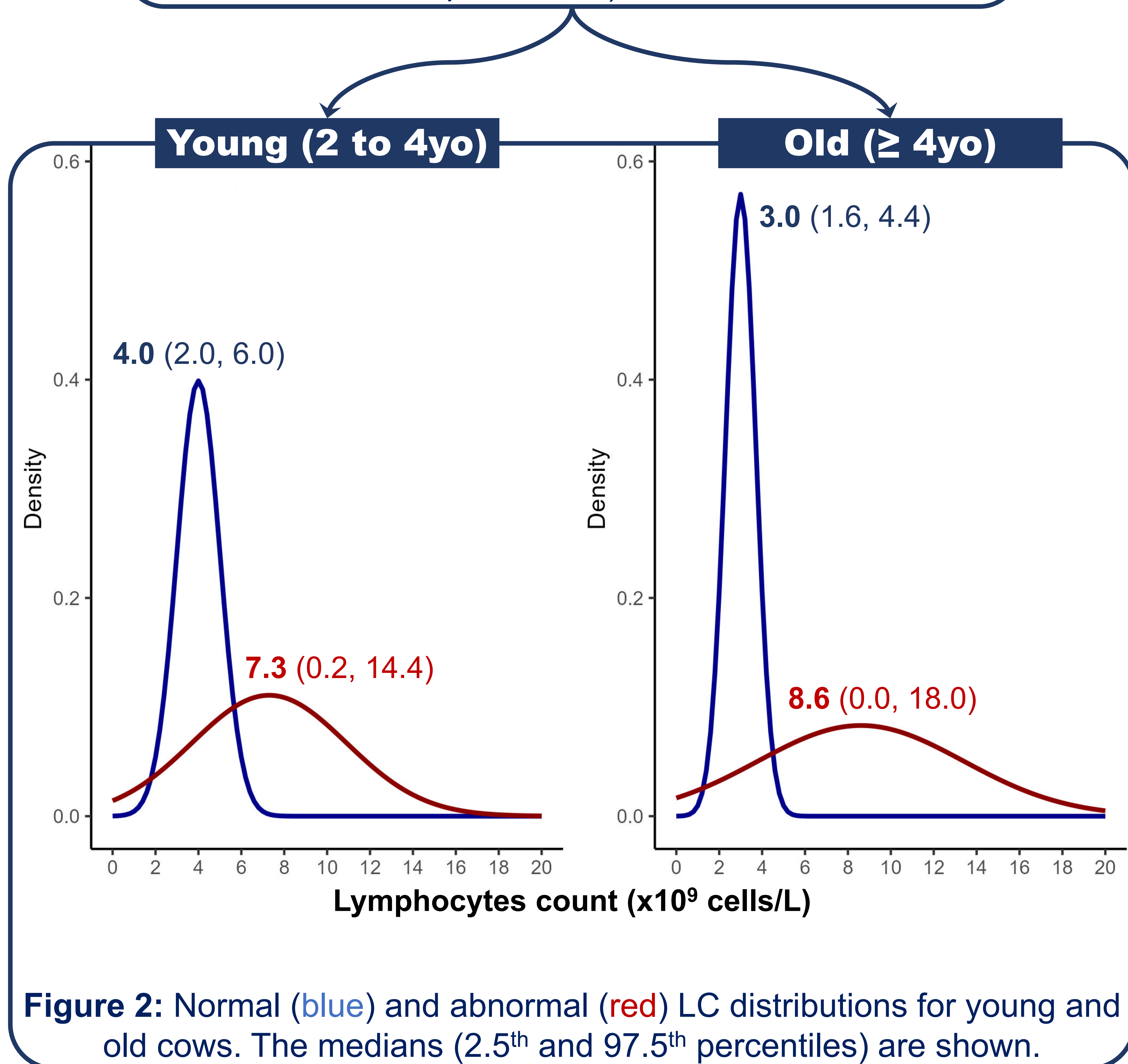
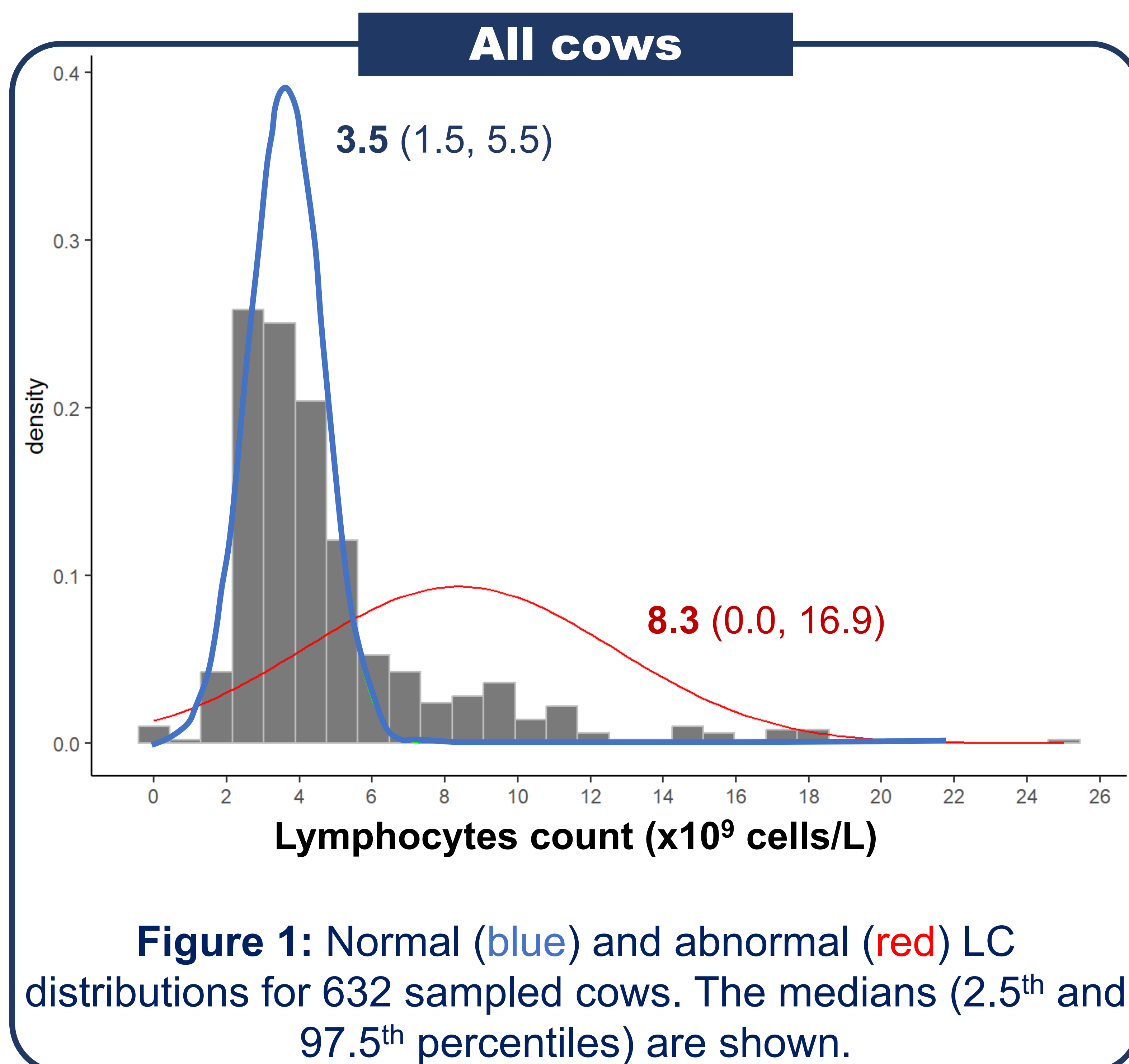
  mu[1] ~ dnorm(5, 0.01) # dnorm(mean, 1/variance) of the whole distribution
  mu[2] ~ dnorm(5, 0.01) # same prior for both distributions

  for (j in 1:2){
    prec[j] ~ dgamma(1,1) # Vague priors for 1/variance
    sigma[j] = sqrt(1/prec[j])
  }

  alpha ~ ddirich(c(1,1)) # Vague prior probabilities for mu and 1/variance
}")
```




RESULTS

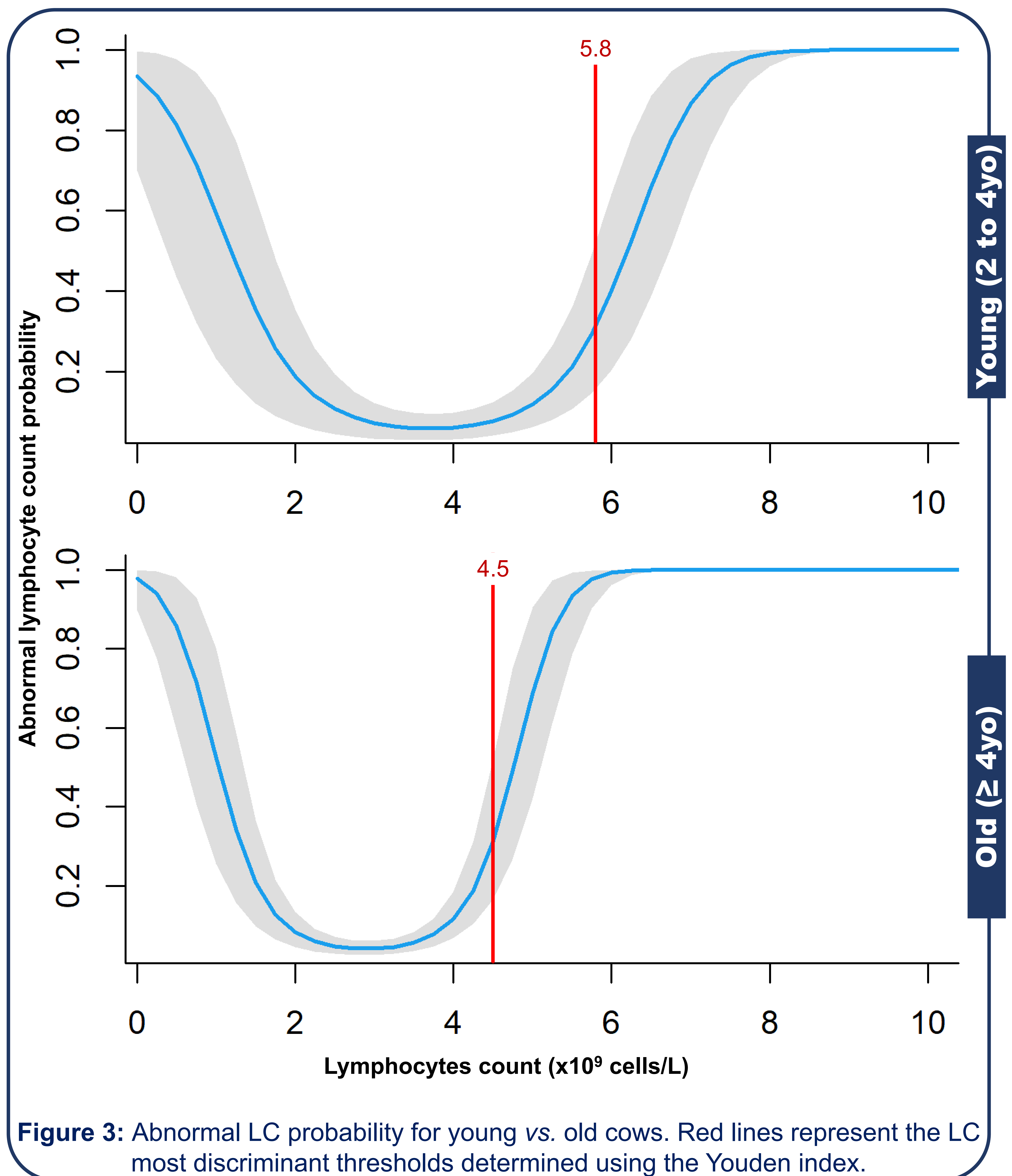


The normal cows LC reference values estimated were higher (2.0 to 6.0 $\times 10^9$ cells/L) in young vs. older animals (1.6 to 4.4 $\times 10^9$ cells/L). In contrast, the LC distributions in the abnormal group were slightly higher in older cows than in younger ones. These results suggest that different LC interpretation thresholds should be used in cows 2 to 4 vs. ≥ 4 year old if this parameter was used to diagnose leukemia.



RESULTS

After generating a list of various LC cut-offs and calculating their corresponding sensitivity (Se) and specificity (Sp), the **Youden index ($Se + Sp - 1$)** was computed to identify the most discriminant LC threshold. The LC cut-offs with the highest Youden index were **5.8 for young** cows and **4.5 x10⁹ cells/L for older** cows. The associated probabilities of having and abnormal LC are illustrated in Figure 3.



Above each LC threshold, the probability of a cow being classified as abnormal (i.e., infected with leukosis) increased. Notably, this probability was also elevated at very low LC levels (0.0 to 0.5 x10⁹ cells/L), suggesting that cows with lymphopenia, may also indicate leukosis (Beyer et al., 2002).



CONCLUSIONS

LC

- ❖ LC in healthy cows was higher in young cows. On the contrary, LC in cows infected with bovine leukosis was higher in older cows.

Threshold

- ❖ Young cows with $LC \geq 5.8 \times 10^9$ cells/L, and older cows with $LC \geq 4.5 \times 10^9$ cells/L, could be assumed to be infected with bovine leukosis.

Lymphopenia

- ❖ Cows with leukosis may also develop lymphopenia.

REFERENCES

- ❖ Yang, D. A., & Laven, R. A. (2022). Performance of the StaphGold ELISA test in determining subclinical Staphylococcus aureus infections in dairy cows using a Gaussian mixture model. *Veterinary Medicine and Science*, 8(4), 1632-1639.
- ❖ Beyer, J., Köllner, B., Teifke, J. P., Starick, E., Beier, D., Reimann, I., ... & Ziller, M. (2002). Cattle Infected with Bovine Leukaemia Virus may not only Develop Persistent B-cell Lymphocytosis but also Persistent B-cell Lymphopenia. *Journal of Veterinary Medicine, Series B*, 49(6), 270-277.

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