A BAYESIAN APPROACH TO ESTIMATING THE PERFORMANCE OF A BOVINE VIRUS DIARRHOEA VIRUS ANTIBODY BULK TANK MILK TEST

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Animals persistently infected (PI) with bovine virus diarrhoea virus (BVDV) are the major source for spread of the BVDV infection. Under the Norwegian BVD program, herds with a BVDV antibody positive young stock were suspected to contain PI animals. The ability of the initial screening test – the bulk tank milk (BTM) test to detect herds with antibody positive young stock was crucial for the test-scheme's performance. In this study the operational performance of the BTM test was investigated using empirical data and a Bayesian simulation procedure.

Materials and methods

Following a positive BTM sample – the first test in the applied three-stage annual test scheme – a milk sample from five selected first calvers (FCM) was collected and if this test was positive, a pooled blood sample from five young stock (YS), 8 to 12 (15) months old, was analysed. Herds negative on the BTM or FCM were not YS tested that year. All samples were analysed using an ELISA test kit (SVANOVIR®, Svanova Biotech, Uppsala, Sweden)[1]. The cut-off value for a positive BTM test was a sample-to-positive (S/P) ratio ≥ 0.25.

The true young stock status in the population of dairy herds for a given year, "the gold standard", was unknown. We estimated this based on the assumption that there was only a low probability for a YS infected herds to be missed by two subsequent annual BTM screenings. Based on this, the minimum prevalence was set to the proportion of herds actually testing YS positive, and the maximum was this value plus the number of herds not tested by the YS test in a given year, but found FCM positive or YS positive the subsequent year (hereafter called the aggregate prevalence). The average of the minimum and maximum was chosen as an estimate for the mean percentage of young stock positive herds and also used to define the standard deviation of the prevalence distribution. Graphs mimicking the sensitivity and specificity of the BTM test at different BTM S/P ratios were made based on the S/P ratio for herds testing YS positive in a given year as well as on the value for herds in the aggregate prevalence for that year.

In situations without a gold standard or knowledge about the true status of the disease of interest, Joseph et al.[2] suggested a simulation procedure using Gibbs sampling to estimate test performance. A pre-written S-plus program has been provided (http://www.epi.mcgill.ca/~web2/bstJoseph.html), where the prior distributions for prevalence, sensitivity and specificity (as beta densities) together

with the number of test positives and negatives are required input values (Table 1).

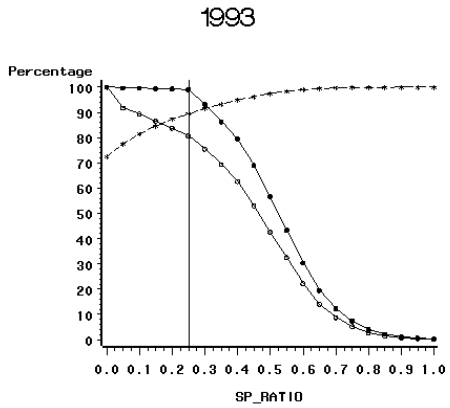
Table 1. The prior distributions with corresponding beta densities (α and β), for the Gibbs sampling simulation procedure.

	Prevalence of YS positive herds		BTM test results	
	Mean, sd	α, β	Positive	Negative
1993	11, 1.5	47.8, 386.4	6 076	20 310
1994	8, 1.5	26.1, 300.0	6 387	19 761
1995	7, 1.5	20.2, 268.2	6 576	19 008
1996	4, 1.5	6.8, 162.9	3 574	21 598
1997	3, 1.5	3.9, 124.5	2 480	22 390
BTM test sensitivity	85, 10	10.0, 1.8		
BTM test specificity	85, 7	21.7, 3.8		

We based our prior assumptions about the expected values for the sensitivity and specificity on literature values[3,4].

Results

The graphs mimicking the sensitivity and specificity (Figure 1) showed a discrepancy between the two positive groups (tested YS positive and aggregated YS prevalence group) for the first years (1993). For the late years (1997) the lines for the two groups come together. It is reasonable to believe that the actual sensitivity should lie somewhere between the lines of these two positive groups.



We also observed that the specificity increased and the sensitivity decreased over the period.

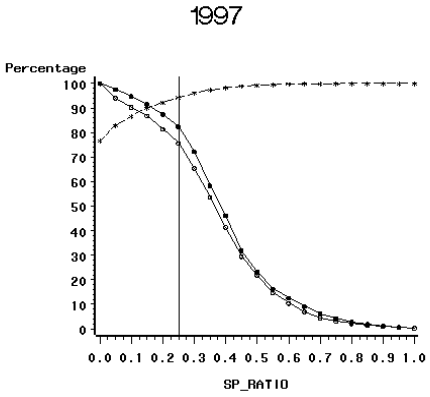


Figure 1, The percentage of young stock (YS) positive herds – in two categories: tested YS positive (•) and tested plus assumed YS positive (◦) – being above a given bovine virus diarrhoea virus (BVDV) antibody sample-to-positive (S/P) ratio as measured by the ELISA bulk tank milk (BTM) test – mimicking the sensitivity, and the percentage of YS negative herds – herds not being in the last category above, being below a given S/P ratio – mimicking the specificity (∗).

The results from the simulation program (Table 2) showed little improvement for the posterior sensitivity estimates. The median values for test sensitivity ranged from 85 to 89%. The median values for test specificity ranged from 79 to 92% showing clearly improved posterior distributions. Differences in specificity, but not for test sensitivity, were indicated between different years (non-overlapping CI's).

Table 2, Gibbs sampling simulation posterior estimates for the performance of the BVDV antibody bulk tank milk ELISA test with respect to the herd young stock status simulated at a sample-to-positive (S/P) ratio = 0.25.

Year	Prevalence		Sensitivity		Specificity		PPV		NPV	
	Med.	CI	Med.	CI	Med.	CI	Med.	CI	Med.	CI
1993	11	8-14	85	51-98	84	80-88	39	22-55	98	93-100
1994	9	6-13	87	61-98	82	79-85	32	19-46	98	95-100
1995	7	4-11	88	62-98	79	77-82	24	14-36	99	96-100
1996	4	2-7	89	63-99	89	87-91	24	11-46	100	98-100
1997	2	1-5	86	60-98	92	91-94	20	7-42	100	99-100

Discussion

Individual animal sampling or direct YS sampling involves considerable expenses. By using BTM sampling as the initial screening tool the cost of disease control programs can be kept low. However, the need for follow up YS testing may, in some populations, be so frequent that the relevance of an initial BTM screening would be questionable.

The sensitivity of the test program will never exceed that of the BTM test. Unfortunately, the BTM test does not separate well the actively infected herds from herds infected earlier, but cleared. The present study indicates that simultaneously high test performance values of about 90 % appears to be the best one can get. Apparently there is an increase in the BTM test specificity and simultaneously a drop in the test sensitivity over the period. This may be related to a shift in the population dynamics (nature of the disease) caused by the BVD program.

The Bayesian approach carries clear weaknesses by not behaving reasonably when the sample size increases and by having a high dependency between the prior and the posterior distributions[5,6]. Also, with low or high prevalences the power for sensitivity or specificity estimation, respectively, will suffer. This is reflected by the simulation procedure failing to predict the drop in sensitivity demonstrated by the graphing procedure. One may be tempted to claim that the simple graphing procedure based on empirical information mimicking the sensitivity, out performs the more technically complex Bayesian Gibbs sampling simulation.

References

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