**Report on the consequences of different design choices of the Bovine TB VIVA trial**

**Introduction**

**Data generated from the trial,**

-Three tests: 1,2,3

-Two populations: A,B

-Two vaccine statuses: +,-

-Sensitivity for each test, under positive and negative vaccination (reference for why this is needed?) (unknown, latent).

-Specificity for each test (unknown, latent).

-Prevalence of BTB for each population (unknown, latent)

-Number of vaccinated and unvaccinated animals in each population (known).

-Number of animals tested positive in each subpopulation for each test (measured)

-Number of animals tested negative in each subpopulation for each test

(measured)

This gives 3\*2\*2=12 measured counts, four known sizes, and 3\*2+2=8 unknowns. This should be an identifiable problem.

**Formal statistical description of the analysis**

Denote by the event that the first two tests, according to a specified ordering, are positive and the third is negative. Denote in a similar fashion the event of all three being positive (), the first and second test negative and the third positive () etcetera. Using this notation, we can write out the probability for a comined test result given population, vaccination status, and infection status, as:

For each triplet belonging to the set of permutations , we have

that :

and

**Considerations of identifiability**

If we assume that specificity of the standard test for vaccinated animals is 0.5, i.e completely unable to distinguish between negative and vaccinated animals, and you allow the sensitivity and specificity to range between 0 and 1, there is a degenerate solution for the above equations where the sensitivity of both the standard and the Viva test is zero, and they always show negative results for positive animals. A solution to this is to require that Sensitivity and Specificity both are above 0.5 (as otherwise flipping the sign would result in a better test) [though is this really the case?? Not sure when combining both Se and Sp…]

**Results**

We generated data assuming that the trial was run on four groups of 5000 individuals each: vaccinated and unvaccinated cattle , from either a high prevalence (modelled as a prevalence of 5%), or a low prevalence (modelled as 2%) population. During a sample run of this scenario, under the assumption that the true sensitivity of the VIVA test was 99.9%, the 95% posterior credible interval for the VIVA test specificity was borderline successful in proving that it was higher than the critical threshold value of 99.4%.

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| --- | --- | --- | --- |
|  | **lower** | **upper** | **True.value** |
| High prevalence pop | 0.0418 | 0.0629 | 0.0500 |
| Low prevalence pop | 0.0134 | 0.0247 | 0.0200 |
| SeStd vaccine pop | 0.6738 | 0.8264 | 0.7000 |
| SeStd nonvaccine pop | 0.6283 | 0.8542 | 0.7000 |
| SeViva vaccine pop | 0.5004 | 0.8329 | 0.7000 |
| SeViva nonvaccine pop | 0.5645 | 0.7569 | 0.7000 |
| SpStd vaccine pop | 0.5437 | 0.5645 | 0.5500 |
| SpStd nonvaccine pop | 0.9943 | 1.0000 | 0.9970 |
| SpViva vaccine pop | 0.9932 | 1.0000 | 0.9990 |
| SpViva nonvaccine pop | 0.9939 | 1.0000 | 0.9990 |

**Recommendations**

**Appendix**