

Estimating diagnostic accuracy of the tuberculin skin test and abattoir meat inspection from bovine tuberculosis surveillance data

AIM : To extend the Bayesian formulation of the Hui-Walter latent class model to estimate diagnostic test parameters and true prevalence of bovine TB from surveillance data

INTRODUCTION

Bovine tuberculosis (bTB): serious disease of cattle

- Causative agent: *Mycobacterium bovis*
- Detection: single intradermal comparative tuberculin test (SICTT), supported by abattoir surveillance (1; figure 1)
- Heritability on the liability scale of SICTT responsiveness
 - 0.14 in Irish and 0.16 in British Holstein-Friesian (HF) dairy cattle (2,3,4)

Diagnostic measures of SICTT accuracy

- Sensitivity (ability to correctly identify infected cattle) ~52.0-100.0% (1, 5)
- Specificity (ability to correctly identify non-infected cattle) ~99.2-99.9% (1, 5)
 - Imperfect accuracy results in misclassification of risk within breakdowns
 - Underestimation of heritability on the liability scale (6)

Aims:

- Extend the Hui-Walter latent class model: Bayesian framework of no 'gold standard' diagnostic test (7)
- Estimate diagnostic parameters and true prevalence from bTB surveillance data & infer true heritability



Figure 1 A-C. Surveillance of bovine tuberculosis (bTB) in Northern Ireland. The single intradermal comparative tuberculin test (SICTT; A) involves separate intradermal injection of *Mycobacterium bovis* and *M. avium* antigens, and works on the premise that *M. bovis*-infected cattle tend to show a greater response to *M. bovis* than to *M. avium* antigens, whereas infection with other *Mycobacterium* spp. promotes the inverse. The SICTT skin change, the difference in response or reaction to the *M. bovis* and *M. avium* antigens, is measured 72 h after injection, whereby the size of the *M. avium* reaction (B) is taken from that of the *M. bovis* antigens reaction. All test reactor cattle are compulsorily slaughtered, and undergo abattoir inspection of animals for tuberculosis lesions at slaughter (C). Furthermore abattoir meat inspection of all cattle at slaughter for tuberculosis lesions is an integral part of the ongoing TB control programme in Northern Ireland.

MATERIALS AND METHODS:

- 1) 73,000 HF dairy cows
- 2) 409 Northern Ireland (NI) HF bTB breakdowns 1995-2010
- 3) Unrecorded data: not all cows with SICTT records had associated abattoir records
 - Excluded abattoir records > 45 days of a positive SICTT result
 - Reason: could not be certain when cows became infected
- 4) Hui-Walter no gold standard latent class methodology extended
 - 2 additional multinomial counts: SICTT +/- cows have no abattoir record
 - Allow for breakdown specific variation in diagnostic sensitivity
- 5) Analyses in WinBUGS and R2WinBUGS package

References

1. De la Rua-Domenech R. et al. A review of the tuberculin tests [gamma]-interferon assay and other ancillary diagnostic techniques. *Res. Vet. Sci.* 2006, 81: 190-210.
2. Bermingham M. et al. Genetics of tuberculosis in Irish Holstein-Friesian dairy herds. *J. Dairy Sci.* 2009, 92: 3447-3456.
3. Brotherton S. et al. Evidence of genetic resistance of cattle to infection with *Mycobacterium bovis*. *J. Dairy Sci.* 2010, 93: 1234-1242.
4. Bermingham M. et al. Evidence for genetic variance in resistance to tuberculosis in Great Britain and Irish Holstein-Friesian populations. *BMC Proc.* 2011, 5: S15.
5. Clegg T. et al. Using latent class analysis to estimate the test characteristics of the interferon-γ test, the single intradermal comparative tuberculin test and a multiplex immunoassay under Irish conditions. *Vet Microbiol.* 2011, 15: 68-76.
6. Bishop S. & Woolliams J. On the genetic interpretation of disease data. *PLoS ONE* 2010, 5: e8940.
7. Hui S.L. & Walter S.D. Estimating the Error Rates of Diagnostic Tests. *Biometrics* 1980, 36: 167-171.

RESULTS

	Estimate (95% BCI)
Sensitivity of the SICTT	0.565 (0.530-0.599)
Specificity of the SICTT	0.999 (0.998-1.000)
Sensitivity abattoir inspection	0.254 (0.234-0.227)
Specificity abattoir inspection	0.999 (0.999-1.000)

Table 1. Parameter estimates of diagnostic accuracy (with 95% Bayesian credibility intervals [95% BCI]) for the single intradermal comparative tuberculin test (SICTT; under 'standard' interpretation, a positive result is recorded when the *Mycobacterium bovis*-antigen response is more than 4mm greater than the *M. avium*-antigen response) and abattoir inspection from the conditional independence model including breakdown specific diagnostic parameter estimates.

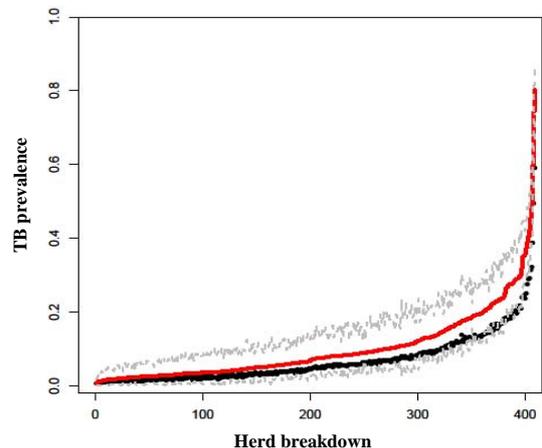


Figure 1. Apparent *Mycobacterium bovis* infection prevalence (black spots) and superimposed estimated posterior mean of true prevalence (red line) with 95% Bayesian credibility intervals (broken grey lines) from the 409 herd breakdowns in this study.

CONCLUSIONS:

- ✓ This study provides an extended Hui-Walter latent class model:
 - Estimation of diagnostic test parameters/true prevalence from bTB surveillance data (Table 1)
 - Assessment of diagnostic test performance at the population level
- ✓ Estimates of test performance are within published range (1,5)
 - Apparent prevalence are likely to be underestimated (Figure 1)
- ✓ Correcting the heritability with diagnostic parameter estimates
 - True heritability estimates for SICTT responsiveness in the GB/Ireland of 0.16/0.19
 - Genetic variation > than initially estimated from surveillance data
- ✓ Extended methodology applications:
 - Epidemiological analysis of other human/animal diseases with incomplete surveillance data for ≥ 2 tests

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