Department
for Environment
Food & Rural Affairs

# Bovine TB testing strategy: optimising the use of current diagnostic tools

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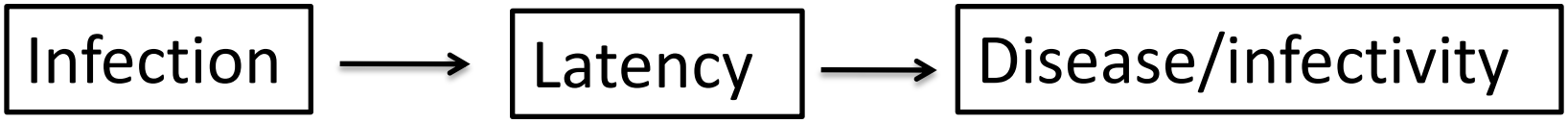
# *Mycobacterium bovis*: the basics

- Member of the *Mycobacterium tuberculosis*-complex (includes the human TB bacterium)
- A resilient pathogen that causes latent intracellular infection and a chronic disease
- Intermittent shedding/infectivity by the host (cattle or badgers)




- Variable duration and timing of each phase
- Immunological assays (such as skin test and interferon-gamma blood test) can detect the host's response to the bacterium in the latent period and before infected animals show any lesions or clinical signs of TB

# Diagnosis of TB in cattle

- Infection with *M. bovis* triggers primarily a cell-mediated immune response in the host
  - Antibody responses in later stages of infection
- Officially approved tests: tuberculin skin test (primary test) & IFN-γ blood test (supplementary tool)
- Assays of humoral immune response (antibodies to *M. bovis* in serum, milk, etc.) have not yet been shown to be significantly better either in humans or in cattle

# Accuracy of diagnostic tests used for disease control

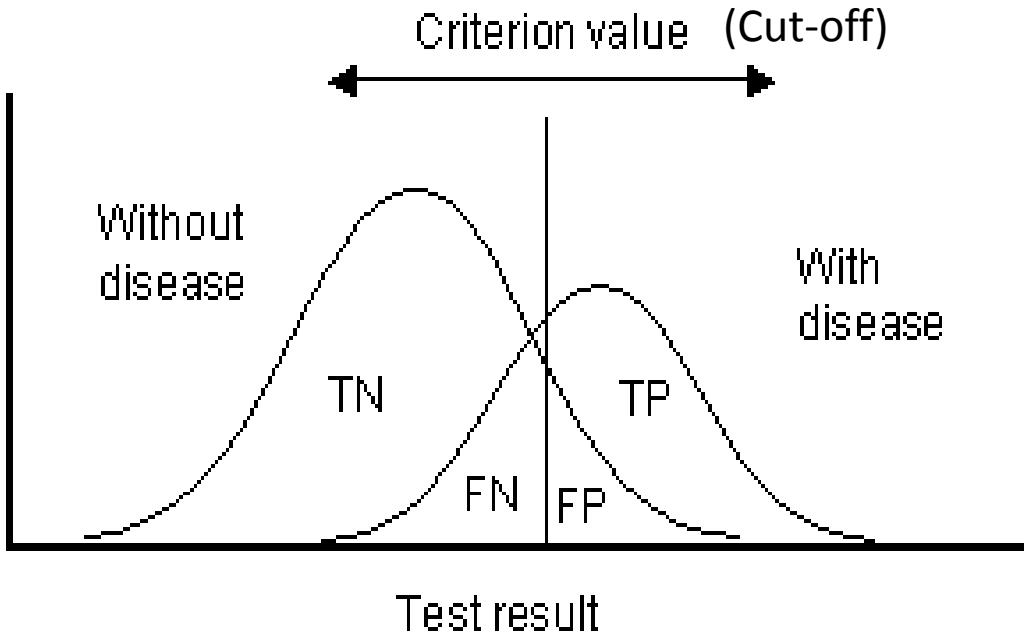
- **Sensitivity (Se)**: probability that an infected animal gives a test-positive result (↑ Se - ↓ % False negative results)

- **Specificity (Sp)**: probability that a non-infected animal gives a test-negative result (↑ Sp - ↓ % False positives)

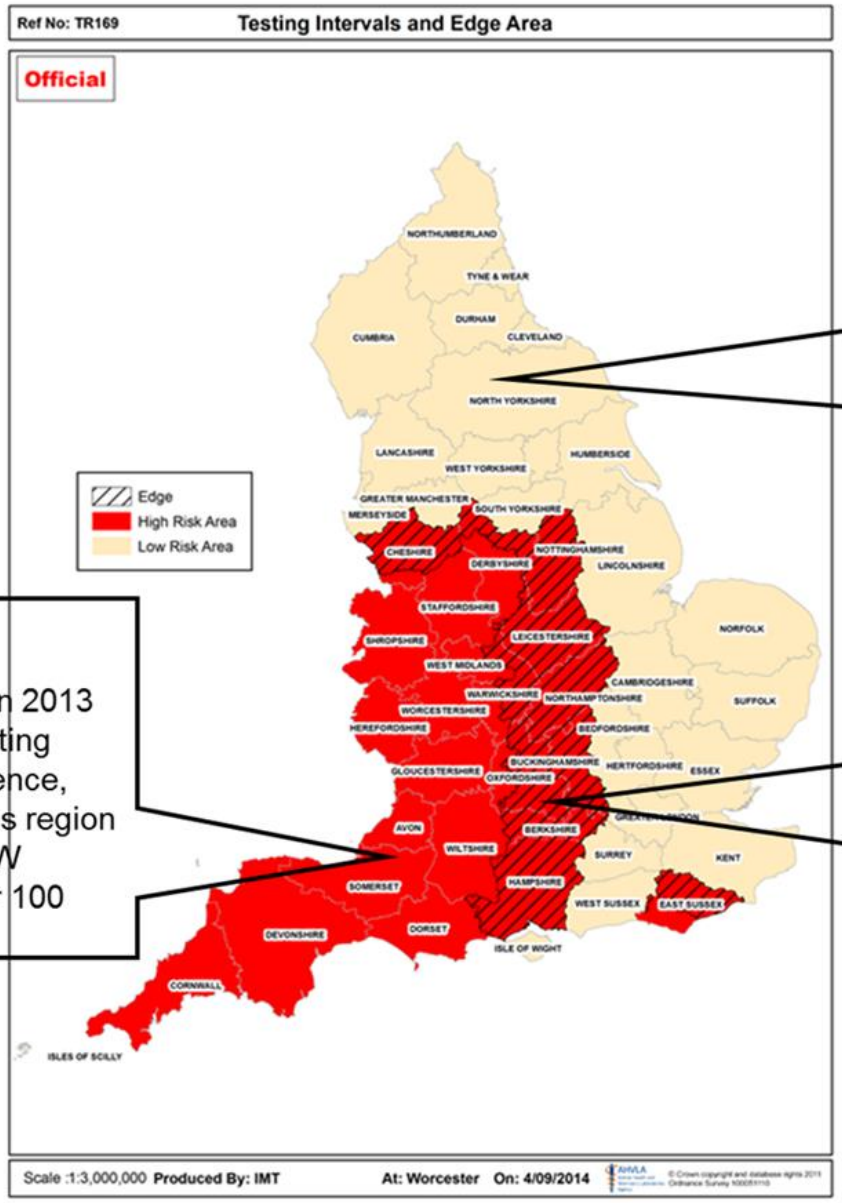
- **Predictive values (PV)**: probability a test-positive animal is truly infected (PV+), or probability a test-negative is free from infection (PV-)
  - PVs vary with the prevalence of infection in the tested group, i.e. is not just about the accuracy of the test
  - help assess options & risks of individual test results

# Diagnostic tests are not perfect!

- Consider effect of false results on assessment
  - Dichotomous outcome (positive/negative) can lead to misclassification of animals
  - Trade-off between Se & Sp: can be varied by shifting the cut-off point depending on the circumstances (e.g. high vs. low prevalence of disease)



# England bTB surveillance and risk areas



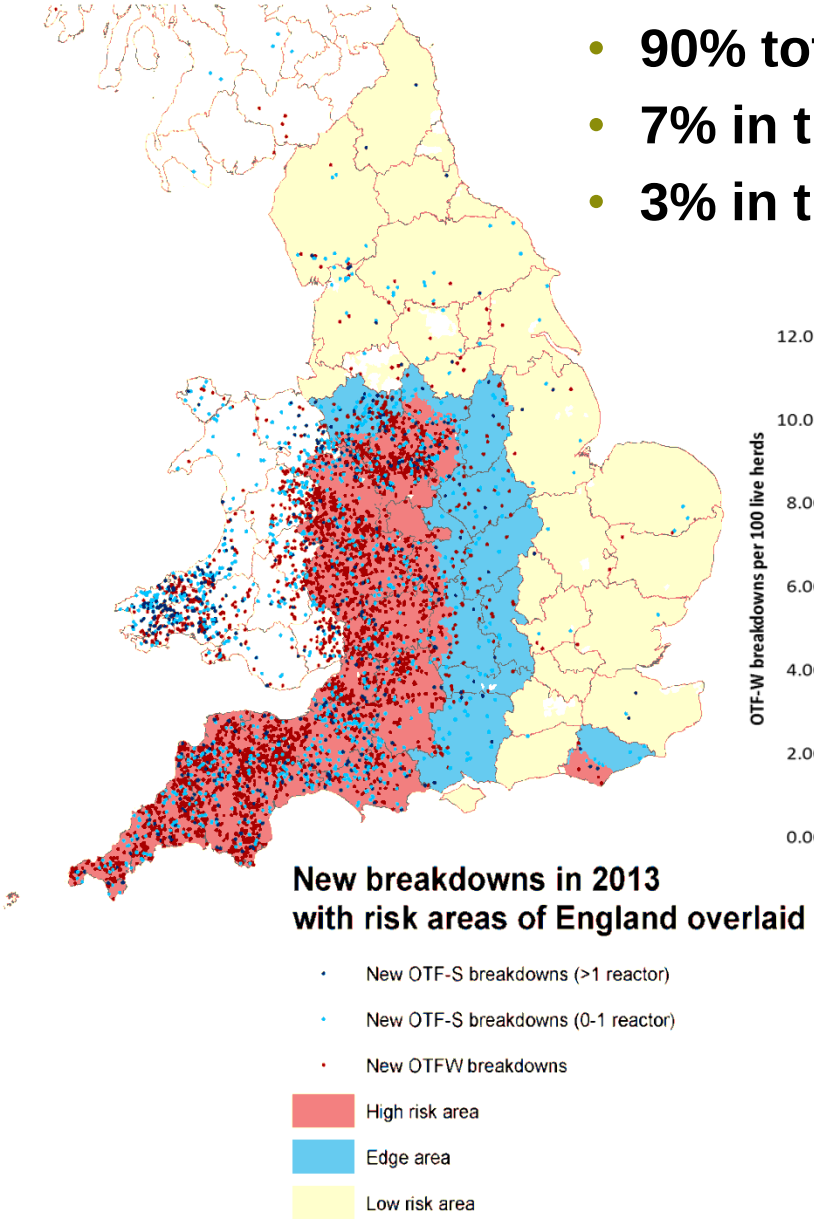

**High risk area**:
38,570 km$^2$
~24,800 herds in 2013
Annual herd testing
High herd incidence, but varies across region (10.6 new OTFW breakdowns per 100 herds in 2013)

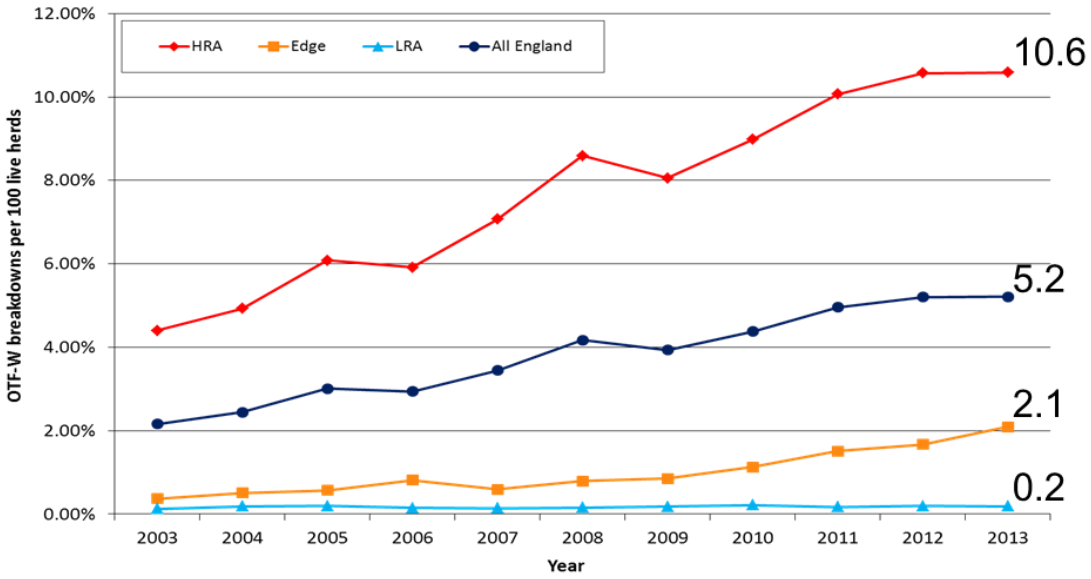
**Low risk area:**
72,621 km$^2$
~21,000 herds in 2013
4-yearly herd testing.
Very low herd incidence (<0.2 new OTFW breakdowns per 100 herds in 2013)

**Edge area**:
21,574 km$^2$
~ 7,800 herds in 2013
Annual herd testing.
Low, but increasing, herd incidence (2.1 new OTFW breakdowns per 100 herds in 2013)

# Incidence of new herd breakdowns (England, 2013)

- **90% total breakdowns occur in HRA**
- **7% in the Edge**
- **3% in the LRA**




**Herd incidence: number of new OTFW breakdowns per 100 'active' herds in 2013, by bTB risk region**

# Performance characteristics of available bTB surveillance methods

| | Animal-level Sensitivity | Animal-level Specificity |
|---|---|---|
| Slaughterhouse surveillance (PM meat inspection + confirmatory lab. culture) | ~ 30% | 99+% |
| Skin test (single intradermal comparative cervical test – standard interpretation) | 81% (95% CI: 70–89%) | 99.98% |
| Skin test (single intradermal comparative cervical test – severe interpretation) | 85% (95% CI: 78–91%) | 99.91% |
| IFN-γ blood test | 91% | 96.6% |

- These are national average values derived from cattle herds in GB
- Actual test accuracy will vary from herd to herd
- Skin test Se can be reduced by poor operator technique, stage of *M. bovis* infection and interaction (co-infection) with other cattle pathogens

# Relative test characteristics for bTB

- Comparative skin test:
  - Highly specific (1 false positive for every 5,000 TB-free cattle tested at standard interpretation), but
  - less sensitive than the single intradermal and the IFN-gamma tests (misses 1 in 4 or 5 infected cattle)
- IFN-γ test: Less specific (3-4 false positives/100 cattle tested), but more sensitive than the comparative intradermal test and easier to quality control
- PV+ for all tests is higher in the HRA, but the skin test's is better
- PV- for all tests is higher in the LRA, but the IFN-gamma test's is better
- So, a higher probability of false positives in the LRA, which would rise with more sensitive tests, but…
- Impact of missing disease is greater in the LRA

# Drivers and constraints

- Bovine TB Strategy for England (April 2014)
- Spending review & cost-sharing options
- Costs and benefits
- Practical delivery/feasibility
- Farmer acceptance
- Maintain cattle trade and EU co-funding/support
- Reduce persistence & recurrence in HRA & Edge:
  - Nearly 60% of breakdowns in HRA occur in herds that have had one or more breakdowns in the past 3 years
  - Residual infection in ~21% of herds regaining OTF status after a bTB breakdown (Cambridge model)

# Approaches already implemented

1. Improved QA of skin testing technique in the field
   - Improved surveillance & breakdown testing sensitivity
   - Enhanced field audit mechanisms for OVs since 2013
   - New procurement system will improve this further
2. Wider usage of IFN-γ test in breakdown situations
   - ↑ testing sensitivity, ↓ breakdown duration, ↓ residual cattle infection, ↓ spread from herds coming out of restrictions, ↓ recurrence rate
   - Default policy for all OTFW breakdowns in LRA and Edge
   - Increasing use in persistent breakdowns in HRA
   - IFN-γ test numbers nearly doubled in 2014 cf. 2013
3. Increased routine herd testing frequency
   - Improved sensitivity of bTB surveillance
   - Earlier detection of infected herds, reduced spread
   - Annual across the Edge since 2013 (6-mo. testing in Cheshire)

# Approaches proposed in the Strategy:

1. Change the skin test interpretation or the type of skin test
   - Can be used to improve Se in both surveillance & breakdown tests
   - Earlier detection of infected animals and herds, reduced risk of spread
   - More severe interpretation of SICCT, bovine-only interpretation, or perform SICT instead of SICCT test in certain high-risk herds or breakdown situations

2. More sensitive short-interval testing procedure for high-risk herds (treat all TB breakdowns in the HRA and Edge Areas as OTFW by default = two SI tests at severe)
   - Improved breakdown testing sensitivity, less residual infection, lower risk of spread form herds as they come out of restrictions

# Approaches proposed (cont.)

3. Wider use of partial and whole-herd slaughters
   - No risk of residual cattle infection, but costly and disproportionate if applied as a blanket policy
   - Must take account of herd re-infection risks from cattle movements and local wildlife
   - Best suited for persistent TB breakdowns in the LRA and serious/persistent breakdowns in the High Risk and Edge Areas, if improved herd biosecurity measures can be implemented to mitigate re-infection risk

# Approaches proposed (cont.)

4. Inconclusive reactors (IRs):
   - In the HRA of England ~24% of IRs detected outside a breakdown situation in 2012 went on to become full reactors, repeat IRs, or showed evidence of infection at routine slaughterhouse surveillance within the following 15 months (the equivalent proportion in the LRA was ~12%)
   - Policy changed from two to one IR re-test (2010)
   - Additionally, could remove all IRs as DCs in breakdown herds and…
   - Ensure that ‘resolved’ IRs could not move from the disclosure herd other than to slaughter (as in RoI)

# Approaches proposed (cont.)

5. Tighten the pre-movement TB testing regime:
   - risky exemptions (movements to shows, common grazing, within SOAs) gradually abolished over 2012-2014
   - compulsory post-movement testing of cattle traded from the annually tested areas to herds in the LRA to live (2015)
6. More severe interpretation of TB spread (forward) tracing skin tests
   - currently done at standard interpretation, with highest TB reactor detection rate (compared with other TB testing reasons)
   - would disclose infection earlier and reduce herd to herd spread
7. Improve routine post-mortem meat inspection of cattle in abattoirs (slaughterhouse cases)
   - responsible for 15% of all new breakdowns in 2013
   - target abattoirs with sub-optimal lesion submission rates

# Challenges

- Can the IFN-γ blood test become a primary screening test for TB in cattle?
- Benefit-cost ratio of doing more IFN-γ testing in the HRA in the absence of wildlife controls?
- Variations in the potency of tuberculin batches: can we replace the ill-defined mixture of antigens in tuberculin with a defined “cocktail” of the key *M. bovis* antigens that would deliver a simpler and more accurate skin test?
- Can the existing antibody-based tests be improved and accepted as supplementary tests for cattle?