Adrian Muwonge DVM, Msc, PhD

Post doc fellow at the Roslin institute

Current research

- Epidemiology of bovine tuberculosis in North western Cameroon
- Molecular epidemiology of tuberculous and non tuberculous mycobacteria in Uganda(2009-2014)
- Molecular epidemiology of M.bovis and M.tuberculosis at the human-livestock interface in Namwala district Zambia(2011-2013)

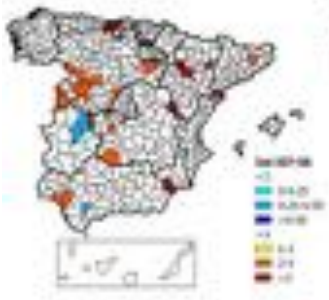
Collaboration

- M.Bovis molecular epidemiology of M.bovis in Ethiopian cattle (2010-2012)
- Pending: Whole genome sequencing of African BTB strains

➢ Current research (national project):

www.cresa.cat

Heterogenous space-time pattern of bTB risk: linked to the presence of bullfighting herds and animal movements from counties with incidence>1%



bTB breakdown investigations

Residual infection	316	39%
Introduction of infected animals	59	7%
Presence of infected goats in the farm	22	3%
Neighborhood infection	85	10%
Sharing of pastures with other infected herds	8	1%
Interaction with wildlife	98	12%
Contact with an infected human	3	0.4%
Unknown	225	28%
Total	816	

- Risk factors for bTB persistence (study on specific areas) ***(in progress)***
- Within farm spread model and evaluation of the current surveillance system ***(in progress)***

➢ Future research (if next national project):

- Role of other domestic animals on bTB epidemiology: goats and extensive reared pigs
- Sociological aspects on bTB eradication
- Risk based surveillance

➢ Support to regional and national government:

Monthly meetings to review the current situation, mapping of disease and helping decision-makers on what actions to take in the affected farms at regional level. Also epidemiological support at national level (courses, development of questionnaires, risk factor study).

CReSA
Centre de Recerca en Sanitat Animal

Andy Mitchell – Data Systems Group (DSG), AHVLA

AHVLA
Animal Health and Veterinary Laboratories Agency

- **DSG are experts in UK bTB Data. In particular:**
  - Making TB data usable by Epidemiologist/Modellers e.g. SAM/VetNet, CTS.
  - A historical understanding of what TB data exists, its uses and its shortcomings e.g. RBCT, BRO, TB99, CCS05 ..
  - Quote from someone present today "*Don't get too precious about bTB data - there is more than enough to go round. It is just a case of doing something sensible with it*"
- **What we do in terms of bTB:**
- **Development work**
  - **Database development**
    - TB99, CCS05, RBCT, BVS, VES …..
  - **GIS Development**
    - Spatial Interactive Disease Atlas (SPIDA), Welsh spatial unit work.
  - **Turning research into policy**
    - Implementation of Glasgow research for the Scottish TB exemptions
- **Data Management**
  - TB99, CCS05, Welsh Found dead study, Woodchester Park,
- **Surveillance**
  - Development of Surveillance reports, Defra consultancy
- **Research**
  - Sub-contractors and joint contractors on many TB research projects
  - Working with (amongst others) CIDC, Warwick, ERGO and Glasgow with regard to their data requirements

Maisons-Alfort Laboratory for Animal Health

- National Reference Laboratory
- Epidemiology unit

- Improvement of direct and indirect diagnostic: PCR, γ-interferon
- Characterization of strain virulence (in vitro and in vivo)
- Characterization of wildlife and environmental reservoirs (lesions score, mathematical modeling, ELISA in wild boars, PCR in the environment)
- Study of husbandry practices in relation to bTB evolution (1965-2000): spatio-temporal analysis of incidence rate, mathematical modeling
- Determination of infection risk through animal movements
- Determination of infection risk factors for recidivist herds

RUTH RUSHTON FORENSIC AND CLINICAL PSYCHOLOGIST

INITIAL FRAMEWORK – RULE BREAKERS AND RISK TAKERS IN FOOD CHAINS

INDIVIDUAL FACTORS

- **Physical attributes**
  - Age
  - Gender
  - Size, weight
- **Personal Characteristics**
  - Personality Variables
  - Temperament
  - Self esteem
  - General health beliefs
  - General beliefs about risk- taking/offending
- **Resource base and livelihood options**
- **Historical experiences**

SOCIAL/PHYSICAL ENVIRONMENT

- **Family and social network**
  - Rules and enforcement
- **Cultural practices**
  - Informal/cultural codes/rules of behaviour
- **Economic drivers**
  - Rules of transactions
  - Methods of enforcement
- **Official rule structures**
  - Methods and willingness to enforce
- **Political environment**
- **Availability and type of information**

INDIVIDUAL ATTITUDES BELIEFS MOTIVATING FACTORS

GROUP HELD ATTITUDES BELIEFS MOTIVATING FACTORS

INDIVIDUAL/GROUP RISK BEHAVIOUR FOR SPREAD OF DISEASE

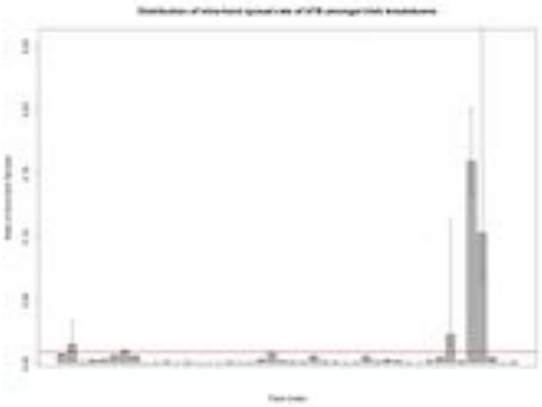
Strong reward motivated – 'conscious' rule breaking e.g. monetary benefit

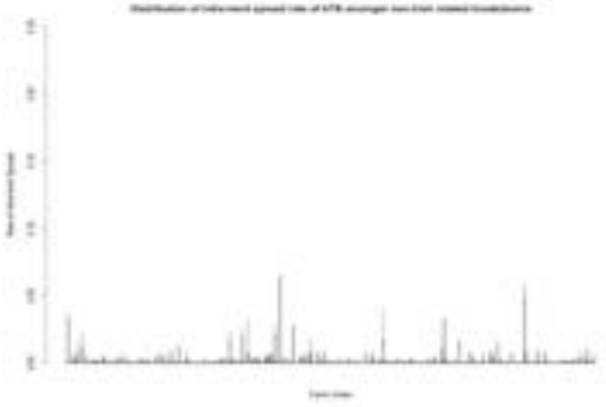
Less 'conscious'/ignorant rule breaking e.g. culturally driven; lack of information

Impact of bTB epidemic under current surveillance strategy

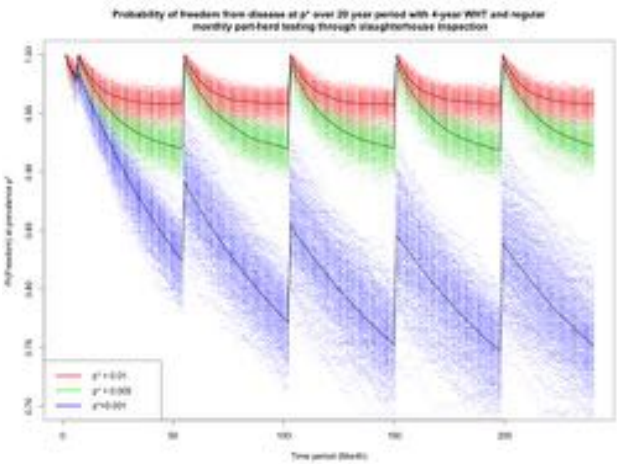
Siben Li, Paul Bessell, Mark Bronsvoort (Roslin Institute)

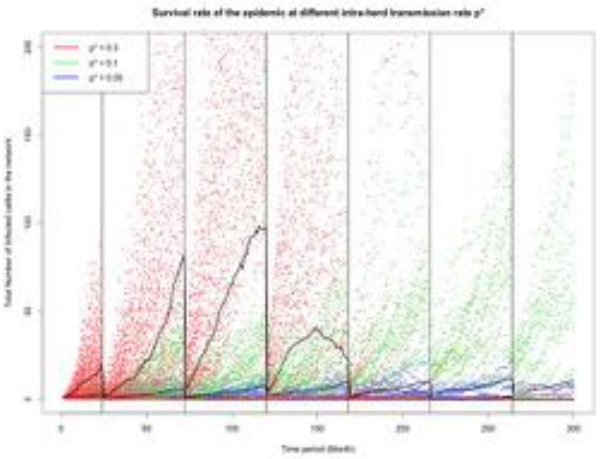
- Analysis of cattle-to-cattle transmission dynamics



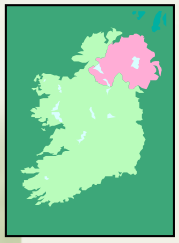


- Analysis of current surveillance strategies for detecting bTB using stochastic simulation models





Department of Agriculture and Rural Development
www.dardni.gov.uk
An Roinn Talmhaíochta agus Forbartha Tuaithe
Mànaidsteri o Fàirms an Kintra Fordèrin



- **TB Trends in UK and Ireland**
- **Epid. meaningful TB parameters**
- **Programme-related risk factors for recurring breakdowns**
- **Epid. significance of TB lesions in cattle**

↑ sun!!

Anita Michel:

- **NTM in cattle & buffalo**
- **Genotyping (Molecular Epid.)**
- **Host immune responses in cattle & buffalo**

↑ rain!!

Darrell Abernethy
Dept. Vet. Tropical Diseases
Faculty of Vet. Science
University of Pretoria

DA:

- **TB Epi – wildlife/human interface??**
- **Programme optimisation in resource-constrained environments??**

James Wood

Ellen Brooks-Pollock

Andrew Conlan

TJ McKinley

UNIVERSITY OF CAMBRIDGE

Department of Veterinary Medicine
Cambridge Veterinary School

Disease Dynamics Unit (DDU) carries out a multi-disciplinary programme of research using classical epidemiological analyses, statistical and mathematical modelling. We have a particular focus on understanding cattle transmission and controls and estimation of complex epidemiological models from herd to national level.

- **Within herd persistence of bTB within herds** (All)
  - Herd size only clear predictor of recurrence and prolongation (Prev Vet Med 92, 360-365, Prev Vet Med 97 (3), 183-190; Prev Vet Med 102 (1), 22-29)
  - No long-term benefit of badger culling on recurrence or prolongation in RBCT areas (PloS one 7 (12), e51342)
- **Estimation of efficiency of cattle controls** (Conlan, McKinley)
  - First estimate of hidden burden of infection missed by testing (PLoS Comp Bio 8 (10), e1002730)
  - Used whole herd slaughters to estimate relative sensitivity of SICCT (PLoS ONE 7(8): e43217)
- **Demography and age structure** (Brooks-Pollock, Conlan)
  - Cattle aged 2-4 years experience highest force of infection
  - Assessment of cattle vaccination strategies
- **National level predictive models** (McKinley)

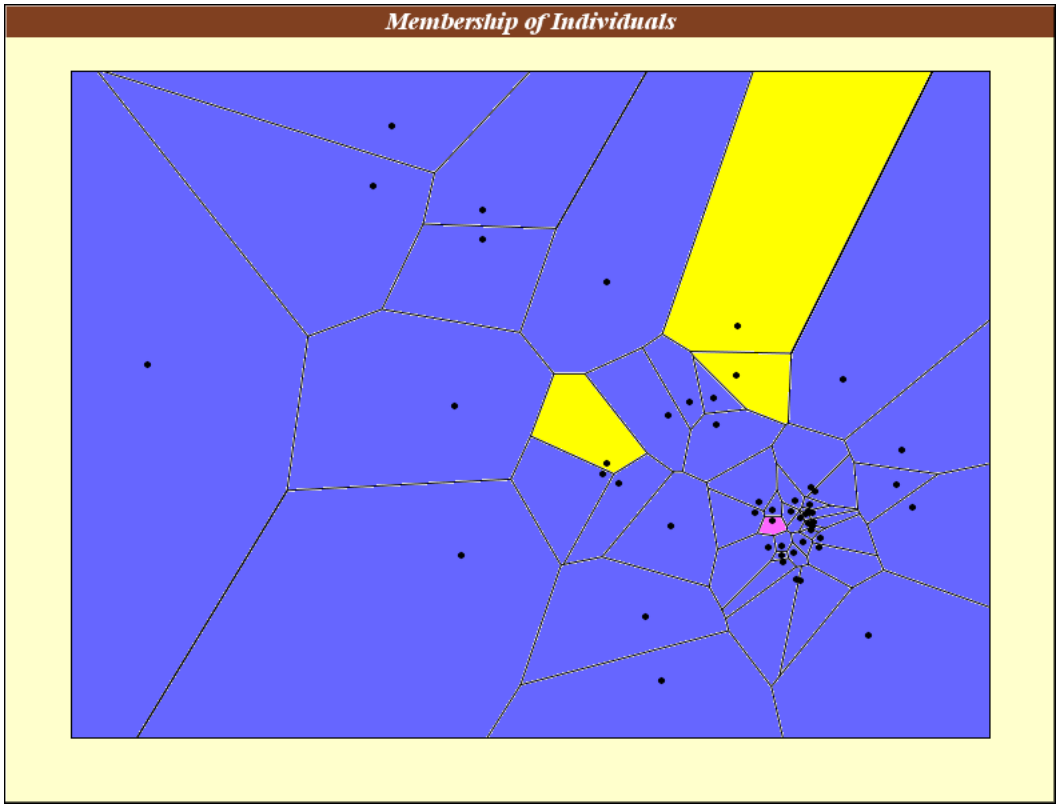
Funding: Defra, BBSRC, EPSRC

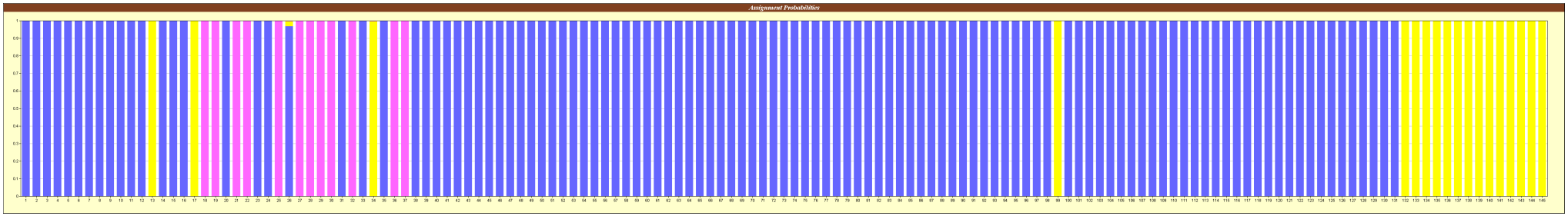
University of Glasgow

Michael Deason
Boyd Orr Centre for Population and Ecosystem Health
Institute of Biodiversity, Animal Health and Comparative Medicine
College of Medical, Veterinary and Life Sciences

Research interests

- Population genetics of whole genome bTB data
- Exploring the fine scale spatial genetic structure of bTB in Great Britain and N. Ireland
- Development of genetics-lead risk assessment strategies





Robin Skuce – PI @AgriFood and Biosciences Institute (Afbi), Belfast

- Afbi - the major science service and research provider for DARD(NI)
- PI – mostly bovine TB molecular biology research
- Lab confirmation of field and abattoir diagnosis in Statutory TB
  - Specialist mycobacterial culture (ISO17025 accredited)
  - Molecular confirmation by spoligotyping (ISO17025 accredited)
- Developed and validated molecular epidemiology tools (MLVA) to investigate bovine TB epidemiology, population structure and evolution (collaboration with AHVLA)
  - Molecular typing surveillance = all TB cases
- Investigating the impact of host and pathogen genetic variation on bovine TB susceptibility (Roslin-led)
- Investigating bovine TB transmission dynamics using molecular typing, mathematical modelling and bacterial-whole genome sequencing (Glasgow-led)
- Bacteriology Branch:
  - Experimental infection models
  - TB cellular immunology, IFNg, sub-unit vaccine/adjuvant, co-infections
  - Badger sett survey, ecology, genetics

Role of AHVLA in bovine TB control for GB govt.

AHVLA
Animal Health and Veterinary Laboratories Agency

- Advice on the development of control policy (V&SPA)
- field implementation of policies (AHVLA Operations)
- Research to elucidate the answers to key questions that arise (V&SPA; VLA, inc Weybridge ESRG)
- Epidemiology and modelling to describe and explain current, and predict future, occurrence (VLA, inc Weybridge ESRG; London ESRG)

Increasing focus on epidemiology and the value of considering the heterogeneous nature of the epidemic to inform control measures

London-based AHVLA staff: policy advice & overall epi input

AHVLA
Animal Health and Veterinary Laboratories Agency

- Synthesis & provision of vet and sci advice to policy makers (Malla Hovi, Ele Brown, Ricardo de la Rua, Wendy Middleton, Rebecca Jones).
  - UK bTB eradication plans, new bTB strategy for England, pilot culls etc
- ICF for Defra's bTB R&D procurement & outputs & secretariat to Defra's independent bTB advisory groups (James McCormack and Susan Campbell)
- ICF to Defra for the dev of badger and cattle vaccines
- Integration of epi and other knowledge from AHVLA field and research, with surveillance data and an understanding of policy, to better understand where control measures are working and where challenges lie (led by Jane Gibbens)
  - Group cases (exposure risk), hypothesis generation, compliance, integrated reporting widely shared, short term disease control objectives?, improve field data capture (some cases), even more focus on misclassification

EUROPEAN UNION REFERENCE LABORATORY
FOR BOVINE TUBERCULOSIS
COMMISSION REGULATION (EC) No 737/2008

VISAVET-EU-RL

Javier Bezos DVM, PhD

Mycobacteria Unit:

· Improvement and development of diagnosis protocols for tuberculosis and paratuberculosis.
· Epidemiological studies (molecular characterization and role of wildlife).
· Immunological studies (specificity and sensitivity of current diagnostic tests).
· Vaccination studies (domestic and wildlife).
· Active collaboration in the National Eradication campaigns for bovine tuberculosis. Advisors.

Working programme 2013 EU-RL

1. **Potency test of tuberculins (guinea pigs).**
2. **Set up of a direct extraction technique from tissue samples.**
3. **Comparative tests (Direct extraction/culture – PCR)**
4. **Mycobacteria recovery from different culture media.**
5. **Assessment of IFN-gamma kits.**
6. **Reference reagents: European Standard and other reference reagents.**
7. **World Wide Web page.**
8. **Missions.**
9. **Training of personnel**
10. **Workshop.**

Fraser Menzies, DARD Veterinary Epidemiology Unit

5 epidemiologists & 2 support staff (+ *ad hoc* field staff)

Interrogation of APHIS database

- herd and animal TB test histories
- animal movements & details

Badger road traffic accident survey

Design of a proposed badger intervention trial

- test, vaccinate or remove captured badgers

Cohort study on the risk posed to TB reactor progeny

- Partnership of consultants able to cover all aspects of food and farming issues
- Call off contract to provide specialist advice as required
- Examples are:
  - LA enforcement/farmer compliance
    - Nigel Durnford
  - TB policy/veterinary/delivery
    - John Montague
    - Nick Coulson
- http://www.foodandfarming.co.uk/

University of Glasgow

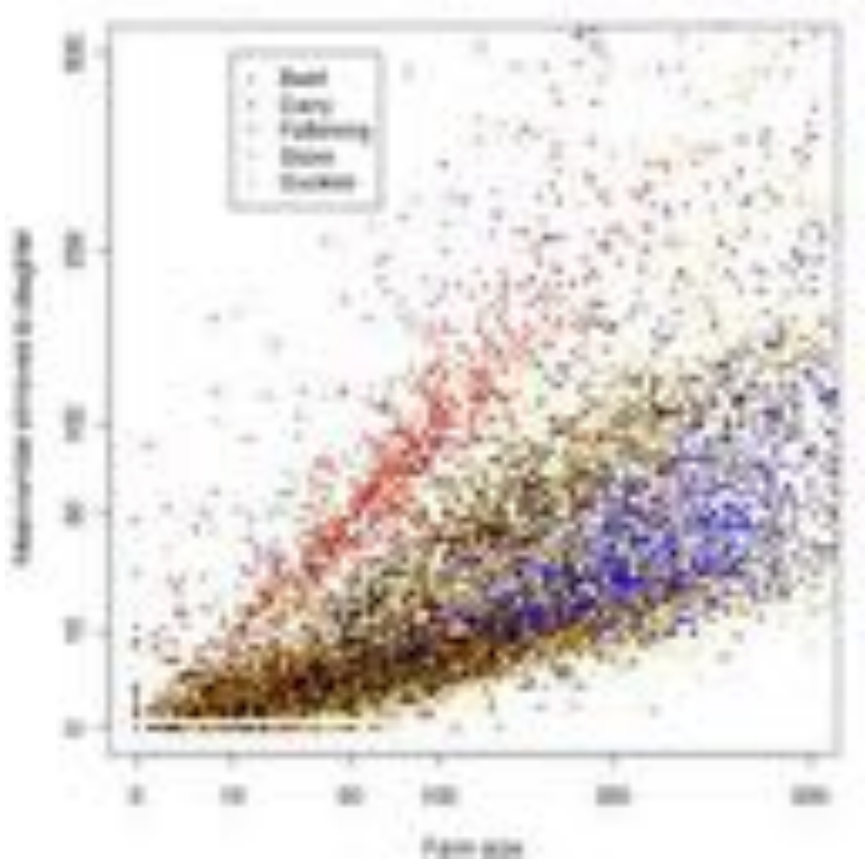
Epidemiol. Infect., Page 1 of 10. © Cambridge University Press 2012
doi:10.1017/S0950268812000635

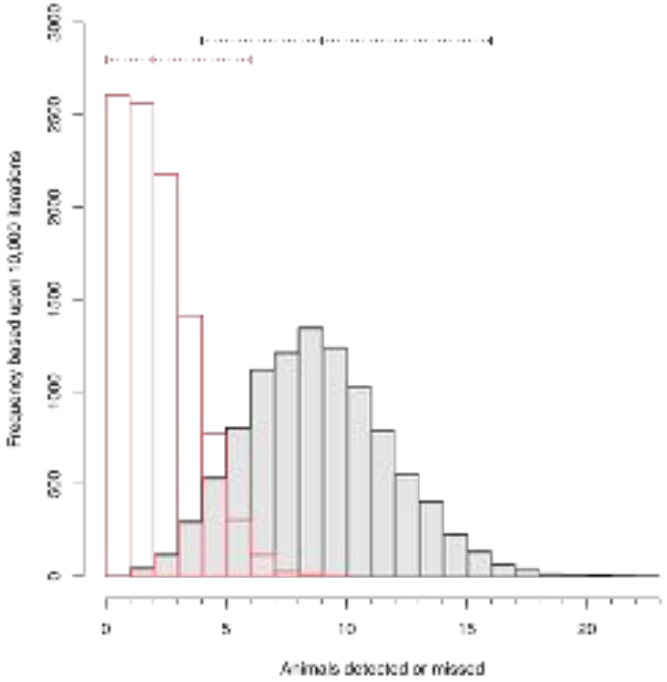
Developing a framework for risk-based surveillance of tuberculosis in cattle: a case study of its application in Scotland

P. R. BESSELL*, R. ORTON, A. O'HARE, D. J. MELLOR, D. LOGUE AND R. R. KAO

ROSLIN epic

Import risk assessment





Philip Robinson

BVMS DSVM MSc MRCVS

2011-2014: PhD: Human geographies of bovine TB control in NI

2007-2011: Veterinary Epidemiology Unit, DARD NI

1999-2007: Veterinary Officer, DARD NI

Robinson PA, Corner LAL, Courcier EA, McNair J, Artois M, Menzies FD and Abernethy DA 2012 BCG vaccination against tuberculosis in European badgers (*Meles meles*): a review *Comparative Immunology, Microbiology and Infectious Diseases* 35 277–287

Atkins PJ and Robinson PA 2013 Bovine tuberculosis and badgers in Britain: relevance of the past. *Epidemiology and Infection,* available on CJO2013 doi:10.1017/S095026881200297

Atkins PJ and Robinson PA 2013 Coalition culls and zoonotic ontologies *Environment and Planning A*, *forthcoming*

Durham University

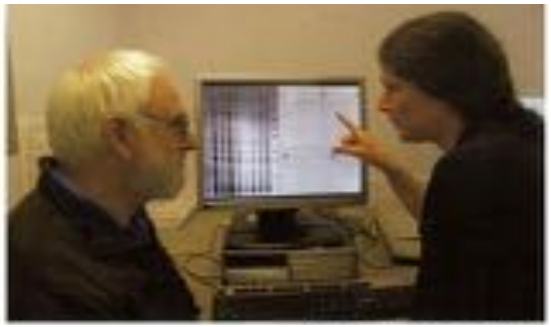
Geoff de Lisle

Herd Testing
(Bovigam ELISA)

***M. bovis* culture**

Paul Livingstone

Strain typing method development



Des Collins

Marian Price-Carter

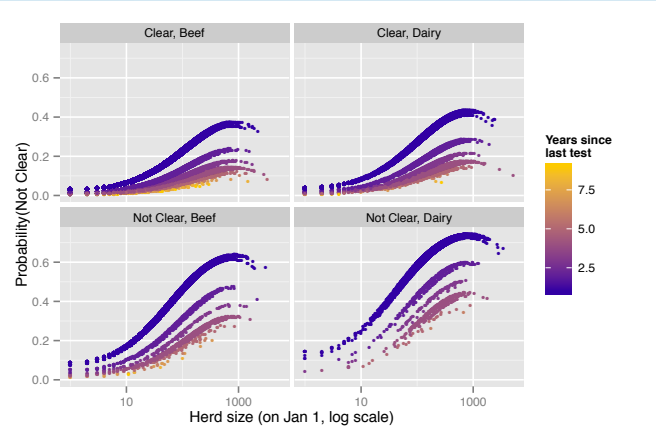
Vaccine development

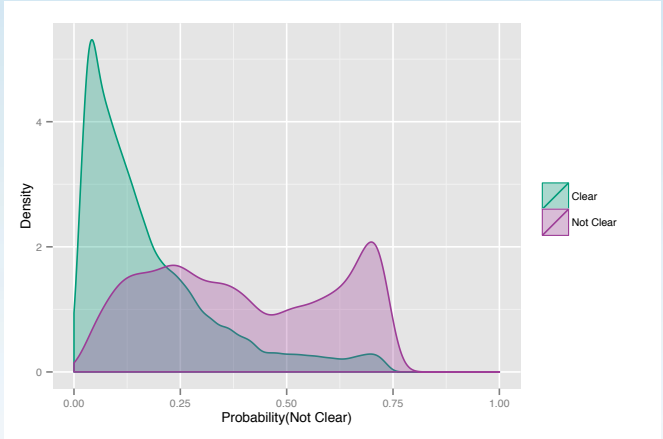
Bryce Buddle

A study to design risk based bTB surveillance regimes

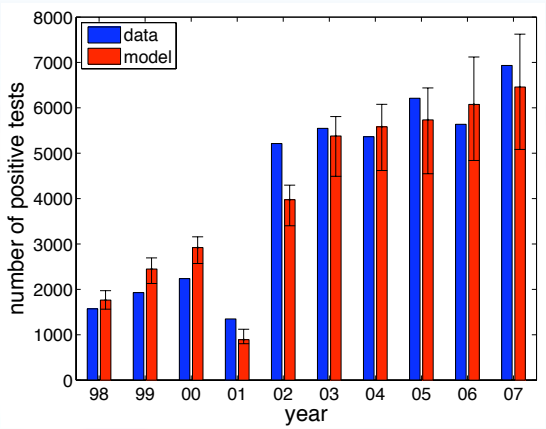
Crump, Brooks-Pollock, Medley & Keeling

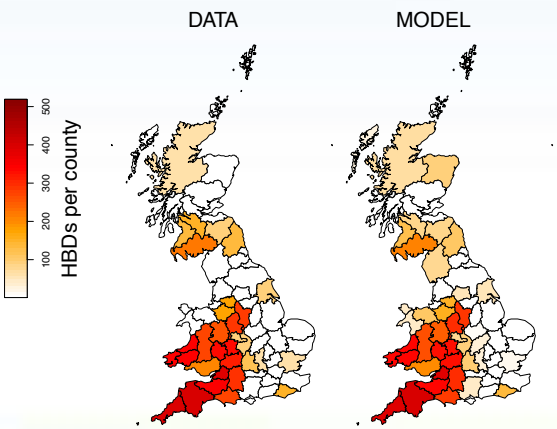
Statistical inference

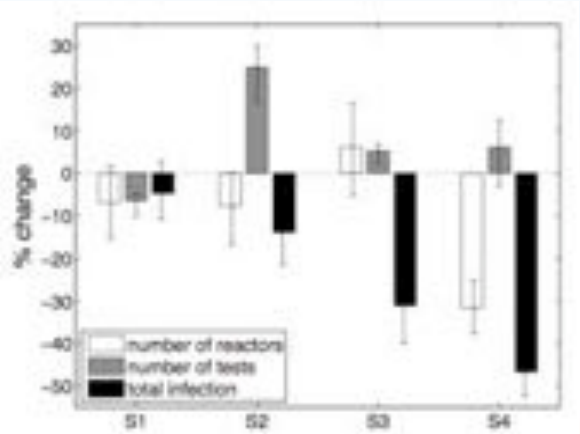




Predictive Modelling







Department for Environment Food & Rural Affairs

r.e.crump@warwick.ac.uk

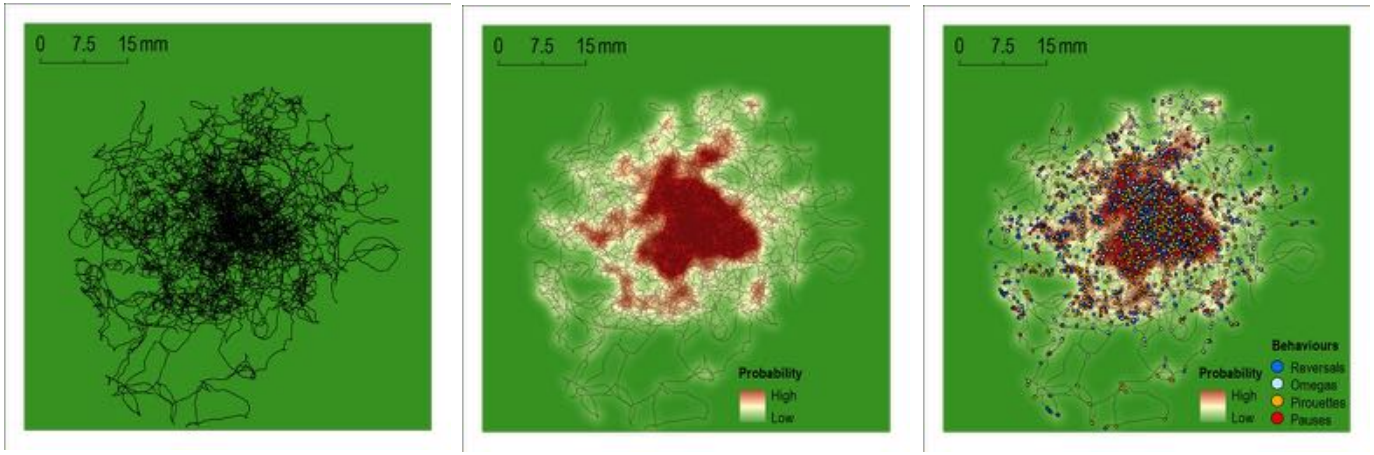
WARWICK

Rowland Kao

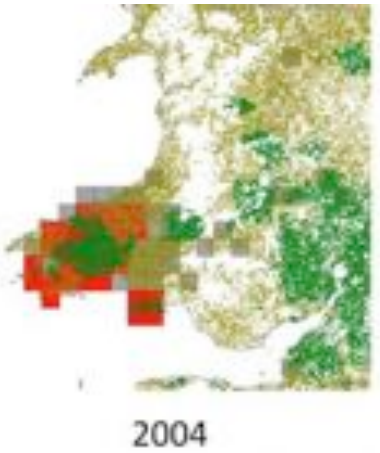
Physics

- Mathematical models
- Methodological development
- Livestock networks and network analyses
- Bayesian Likelihood parameter inference
- Integration of molecular epidemiology
- Use of combined mathematical and genetic data (‘phylodynamics’)

Liliana Salvador
Boyd Orr Centre for Population and Ecosystem Health
Institute of Biodiversity, Animal Health and Comparative Medicine
College of Medical, Veterinary and Life Sciences



- **Movement signatures of bovine tuberculosis (bTB) spread in Great Britain (GB)**
- **Identification of High Risk Areas of bTB in GB**
- **Spatio-temporal distributions of Mycobacterium bovis**
- **Movement models to study wildlife-cattle interactions**



R.R.Kao, R.J.Orton,P.R.Bessel, D.M.Green, *submitted*

Susanna Sternberg Lewerin

Professor in Epizootiology & Disease Control, SLU

- Chair of TB subgroup of the EU Commission Task Force on disease eradication programmes, part of new review process
- Bacteriologist/Epidemiologist teaching vet students about disease control etc
- Reserch no TB focus, general disease control: animal movement networks, other between-farm contact networks, on-farm biosecurity, (disease modelling)

Thomas Doherty

Background:

- Software Engineer
- Metadata and data management solutions for the ATLAS experiment CERN
- Development of solutions to enable and interface with 'scientific applications' on the GridPP physics Grid (a Grid primarily used for ATLAS and other particle physics experiments)

EPIC Work:

- Development of a generic mega-simulation epidemiological model (Soho) that allows for the processing and analysis of UK wide datasets using the Grid
- It currently runs an individual level (cattle) level model using UK Cattle Tracing System (CTS) data.
  - This involves handling 30 million cattle over a ten year period 2001-2011
  - And the 250 million movements associated with these animals
  - The model is stochastic so needs to be simulated many thousands of times

bTB Work:

- First case study for Soho model is to simulate the spread of bTb through UK cattle herds - comparing simulated results with VetNet data
- Inferring summary statistics using Approximate Bayesian Computation (ABC)

The University of Reading

Veterinary Epidemiology and Economics Research Unit (VEERU)

- Exploration of factors that might explain the spread of the bovine TB endemic area. A report for AHVLA. December 2012.

  Michelle Boath, Ian Dunbar, Nick Taylor and Helen Wilkinson

- Descriptive Epidemiology of Bovine TB in England – 1980 - present. A report for Defra. June 2010.

  Nick Taylor, Keith Allison, James Hanks, Sabine Pflug and Tony Wilsmore

- Bovine Tuberculosis - an update. A report for Defra. October 2007.

  Tony Wilsmore & Nick Taylor

- A review of the international evidence for an interrelationship between cattle and wildlife in the transmission of bovine tuberculosis. A report for Defra. September 2005.

  Tony Wilsmore and Nick Taylor

Epidemiology, Surveillance & Risk Group, AHVLA-Weybridge UK

Regular TB surveillance reports for England, Wales and Scotland

- Surveillance reports with innovative statistical analyses, and specialised surveillance studies in Wales
- Supporting the delivery of the bTB eradication programme throughout GB with epidemiological advice on interferon-gamma testing and pathological sample reporting

Transmission and spread studies

- Mapping and explaining the rate of spread of endemic TB in Britain, working alongside GIS analysts, social scientists, official veterinarians, private veterinarians, and farmers
- Spatial distribution of TB genotypes in cattle & badgers in Wales (involving regional labs)
- Risk-based trading project, including development of a tool for estimating the probability of *Freedom From Infection* (FFI) of herds, which continuously updated from test, movement and local exposure data
- Using Home Ranges for tracing the probable provenance of *M. bovis* genotypes in breakdowns
- Spatio-temporal analysis of reactive culling in the Randomised Badger Culling Trial, calculating environmental risk factors

Evaluation of test performance

- Effect of changing the interpretation of skin tests in bTB breakdowns on the risk of recurrence
- Evaluation of sources of tuberculin in detecting bTB-infected cattle, using surveillance data
- Multi-participant meta-analysis of sensitivity & specificity of tests for TB, with evaluation of reporting quality
- Evaluating Interferon-gamma DIVA tests – Differentiating Infected from Vaccinated Animals (cattle)

In addition to research, AHVLA operates a diagnostic laboratory for identifying and genotyping *M bovis*, acting as the National & OIE reference laboratory

AHVLA has a network of regional labs and divisional animal health offices, involved in detection and diagnosis of bTB and other diseases. They help to acquire data and samples for research projects such as field trials

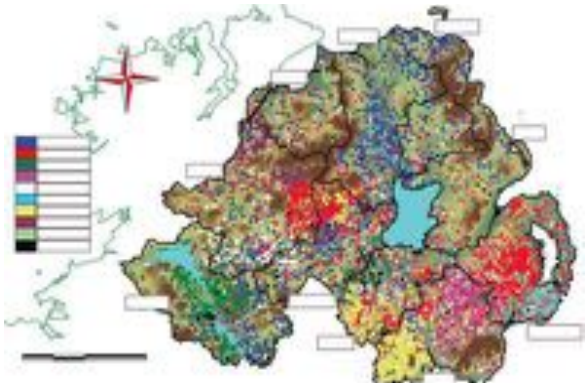
The People:

- **ESRG: Amy Adkin,** Jenny Broughan, Adam Brouwer, Lucy Brunton, Sara Downs, Elizabeth Ely, Tony Goodchild, Kate Harris, Jo Lawes, Jessica Parry
- **Other teams in AHVLA:** Adam Ashton, Mark Chambers, Rachel Eglin, Gareth Jones, Rose Nicholson, Shelley Rhodes, Noel Smith, Paul Upton, Martin Vordermeier
- **Major external collaborators:** Angus Cameron, Gareth Enticott, Matthias Greiner, Steve Hinchliffe, Damain Maye, Javier Nuñez, Kim Ward, William Wint & ERGO

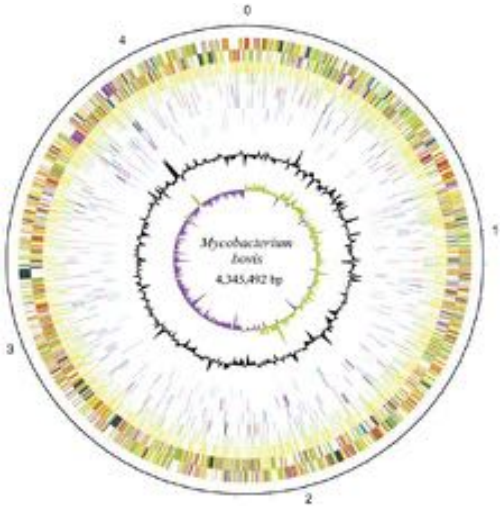
University of Glasgow

Hannah Trewby

- Whole genome sequencing to investigate the fine scale transmission dynamics of bTB in the UK
  - Increased resolution cf. strain-typing
- Currently - Northern Ireland
  - Cattle-focused data
- Woodchester Park collaboration
  - Badger side of the story
- Sequence assembly and SNP-calling
- Combine genetic and epidemiological information



Skuce *et al.* 2010 Vet Rec



Garnier *et al.* 2003 PNAS

Jan Muskens

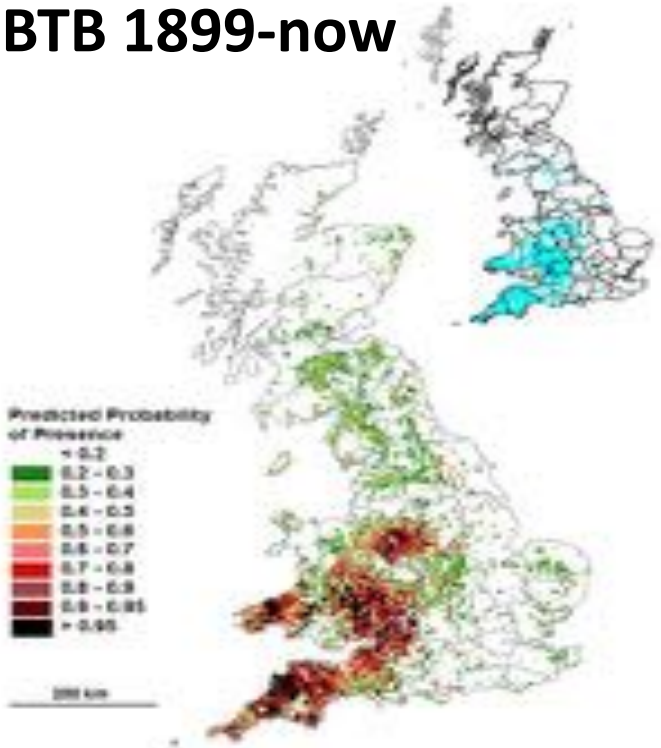
- Veterinarian, cattle health specialist
- Animal Health Service (AHS), Deventer, The Netherlands
- PhD: paratuberculosis in Dutch dairy herds (diagnosis and epidemiology)

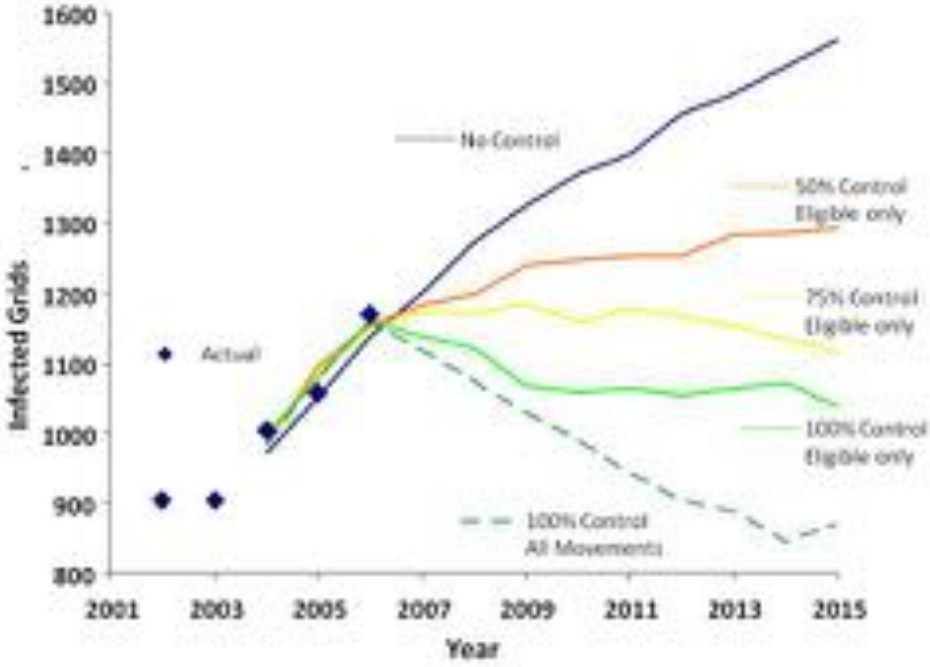
My work in bovine tuberculosis (tb):

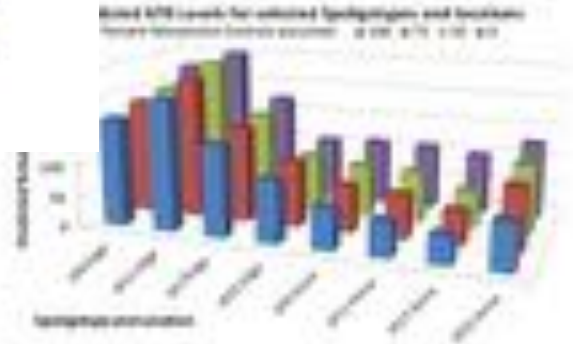
- Earlier: AHS was responsible for national bovine tb program; organizing this was part of my job (together with other specialists)
- Nowadays:

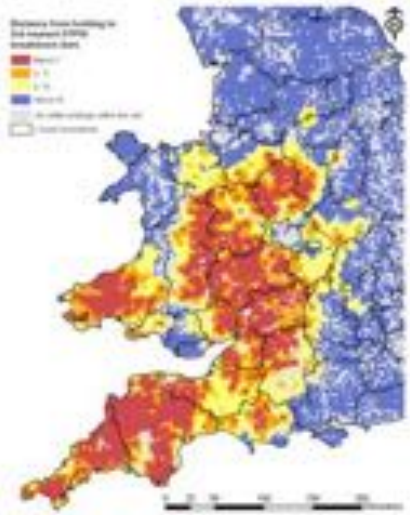
- informing farmers and veterinarians about topics of bovine tb in the Netherlands and outside: outbreaks, diagnosis, studies, etc.
- together with epidemiologists: estimating risk of import and transmission between herds and how to minimize these risks

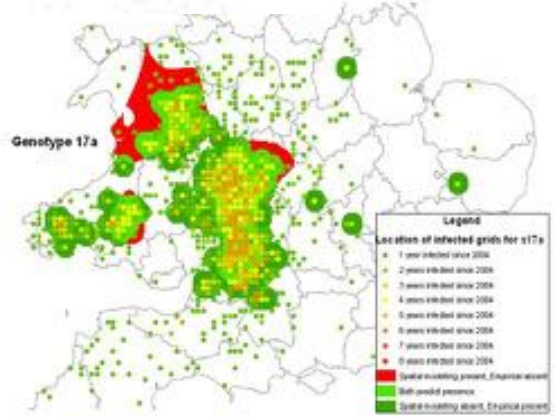
William Wint et many al.
BTB 1899-now











Royal Veterinary College
University of London

Julian Drewe

1. Cleverer use of diagnostic tests in live animals
2. Contact patterns between badgers and cattle
3. Comparative epidemiology
4. Targeted control of infection