The Centre for Veterinary Epidemiology and Risk Analysis

The TB Diagnostics and Immunology Research Laboratory

Biennial Report, 2018-19

UCD DUBLIN

An Roinn Talmhaíochta,
Bia agus Mara
Department of Agriculture,
Food and the Marine

The Centre for Veterinary Epidemiology and Risk Analysis

The TB Diagnostics and Immunology Research Laboratory

Biennial Report, 2018-19

S.J. More and D.M. Collins (editors)

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ISBN: 978-1-910963-43-2

Preface

The Department of Agriculture, Food and the Marine (DAFM) provides ongoing financial support to two research units within the UCD School of Veterinary Medicine at University College Dublin:

- The UCD Centre for Veterinary Epidemiology and Risk Analysis (UCD CVERA); and
- The TB Diagnostics and Immunology Research Laboratory

These units each work to support DAFM policy, inspectorate and laboratory staff in the area of animal health. The TB Diagnostics and Immunology Research Laboratory focuses on bovine tuberculosis research. UCD CVERA is a national resource centre, providing policy advice and conducting epidemiological research on a wide range of animal health issues. In addition, UCD CVERA provides general support to government, industry and the veterinary profession (pre- and post-graduation).

This report documents work conducted by, or in association with, these UCD-based research units during 2018 and 2019.

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Acknowledgements

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- DAFM State Veterinary Service
- DAFM Veterinary Laboratory Service
- Animal Health Ireland
- Campaign for Responsible Rodenticide Use Ireland CLG
- Cork Institute of Technology
- Ecolab Ireland
- Emel Consulting
- Farmlab Diagnostics
- Irish Cattle Breeding Federation
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- Marine Institute
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- Teagasc
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- Wildlife Conservation Research Unit, Department of Zoology, University of Oxford, The Recanati-Kaplan Centre, Tubney, Abingdon, Oxfordshire, England
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- Department of Medicine & Epidemiology, School Veterinary Medicine, University of California, Davis, California, USA
- Kansas State University College of Veterinary Medicine, Manhattan, Kansas, USA
- NOAA/Air Resources Laboratory, College Park, Maryland, USA
- Transboundary Epidemiology Analytics, LLC, Fort Collins, CO, USA

The TB Diagnostics and Immunology Research Laboratory

Gamma-interferon (IFN-γ) blood testing and research

Staff from the UCD laboratory acknowledge the help and support of Regional Veterinary Office (RVO) staff in providing samples for the IFN-γ test.

Badger Vaccine development

Staff working on the Badger Vaccine Project acknowledge the contribution and support of Kevin Kenny, Naomi Fogarty and colleagues at the mycobacteriology laboratory (DAFM Veterinary Laboratory Service, Backweston, Celbridge, Co. Kildare, Ireland), and Paddy Sleeman of University College Cork for fieldcraft. Sandrine Lesellier (ANSES, France) and staff at the Animal and Plant Health Association (APHA, Weybridge, England) are also thanked for contributing technical expertise for the research programme.

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TB Diagnostics and Immunology Research Laboratory

Gamma-interferon (IFN-γ) blood testing and research

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Badger Vaccine development

Eamonn Gormley
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Overview

The Centre for Veterinary Epidemiology and Risk Analysis

The UCD Centre for Veterinary Epidemiology and Risk Analysis (UCD CVERA) is the national resource centre for veterinary epidemiology in Ireland, located within the UCD School of Veterinary Medicine at University College Dublin. The Centre was initially established as the Tuberculosis Investigation Unit, but has since broadened its remit to cover a wide range of international, national and local animal health matters, including:

- Epidemiological support for the control and eradication of regulatory animal diseases, including the national eradication programme for bovine tuberculosis, and for emergency animal disease preparedness and response;

- Work in support of Animal Health Ireland (www.animalhealthireland.ie), which is providing a proactive, coordinated and industry-led approach in Ireland to non-regulatory animal health concerns (such as mastitis, bovine viral diarrhoea and Johne's disease); and

- Epidemiological support for a broad range of other animal health and welfare issues relating to animal health surveillance, on-farm investigations, welfare of farmed livestock and horses, health of companion animals and farmed fish, and international collaboration.

UCD CVERA staff work closely with national policy-makers, both in government and industry. Staff also contribute to training in veterinary medicine, both to undergraduates and postgraduates. A broad range of expertise is represented within the Centre, including database development and management, geographic information systems, biostatistics, veterinary medicine and epidemiology. The Centre is staffed by employees of University College Dublin and of the Department of Agriculture, Food and the Marine (DAFM).

During 2017, a strategic review of CVERA took place in conjunction with the Department of Agriculture, Food and the Marine, the UCD School of Veterinary Medicine, Animal Health Ireland and other stakeholders. As a result of the review, CVERA has developed clearly defined strategic goals, objectives and expected outcomes. These are presented in the CVERA Statement of Strategy 2017-20, and are currently being addressed.

For more information please visit: http://www.ucd.ie/cvera/reports/

The TB Diagnostics and Immunology Research Laboratory

The Tuberculosis Diagnostics and Immunology Research Laboratory based at UCD engages in routine IFN-γ testing of blood samples submitted from Regional Veterinary Offices. Arising from the large number of samples tested each year, there is a focus, in collaboration with CVERA, on analysing the data to gauge the performance of the test under Irish conditions and searching for ways to improve the accuracy of testing. The laboratory also liaises with colleagues working in institutions at home and abroad to share knowledge of the test and keep abreast of any new developments that may impact on its performance.

A second key area of work for the laboratory is the badger vaccine programme of research with the objective to use vaccination to control tuberculosis in badgers and to break the link of infection to cattle. In many studies involving captive badgers we have demonstrated that vaccination of badgers with BCG by a number of routes, including oral delivery, generates high levels of protective immunity against challenge with *M. bovis*. The laboratory was also responsible for providing scientific direction to the Co. Kilkenny vaccine field trial. With the implementation of a national vaccination programme underway, the UCD laboratory continues to provide key scientific support to underpin the delivery of the strategy.

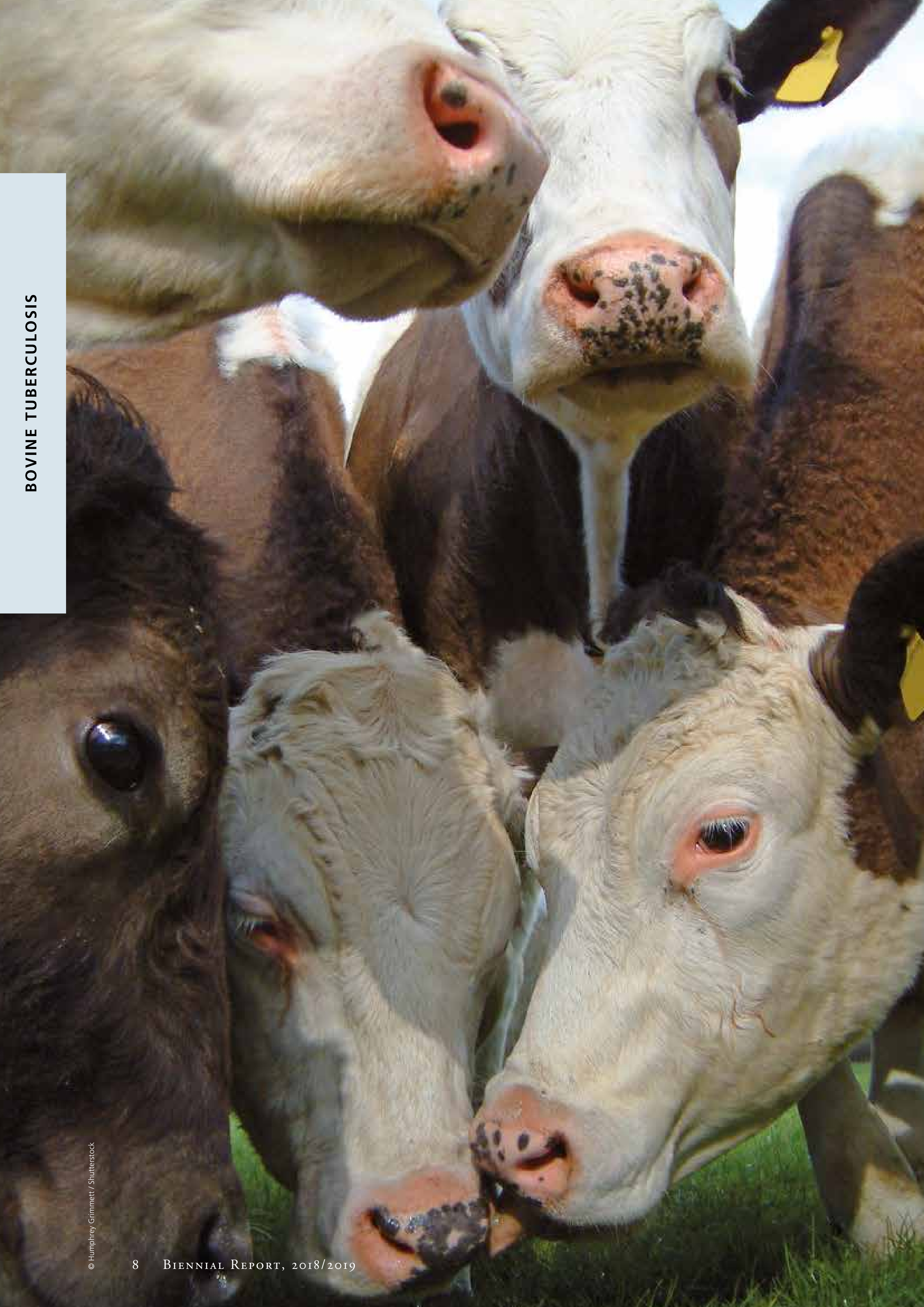
Further information

In this report, projects are either:

- Complete, which includes those projects where relevant peer-reviewed papers, or equivalent, have been published in 2018/19, or

- Current, which includes the balance of active projects covering the spectrum from an advanced research concept through to final write-up or manuscripts in press.

Manuscript preparation is conducted in accordance with Uniform Requirements for Manuscripts Submitted to Biomedical Journals of the International Committee of Medical Journal Editors (previously the Vancouver Group). For further information, see www.icmje.org. Guidelines for the transparent reporting of specific study types (for example, the CONSORT statement for transparent reporting of trials, www.consort-statement.org) are followed. An up-to-date list of all peer-review papers produced by, or in association with, the UCD Centre for Veterinary Epidemiology and Risk Analysis, and /or The TB Diagnostics and Immunology Research Laboratory is available at www.ucd.ie/cvera. Follow us on Twitter @ucd_cvera.



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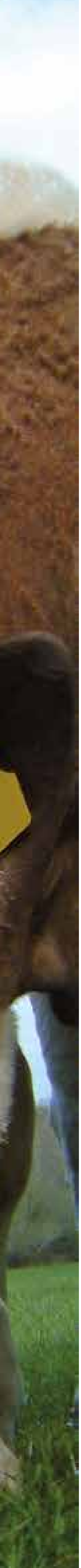

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Bovine tuberculosis

Tuberculosis in cattle

The role of wildlife in bovine TB

Contributing to national TB policy

National maps

Improving surveillance

Field-based surveillance

Characteristics of *Mycobacterium bovis* infected herds tested with the interferon-gamma assay

Clegg, T.A.[1], Doyle, M.[2], Ryan, E.[3], More, S.J.[1], Gormley, E.[2]

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Preventive Veterinary Medicine 168, 52-59 (2019)

The IFN-γ (interferon gamma) assay is used in Ireland as an ancillary diagnostic test to the single intradermal comparative tuberculin test (SICTT) to maximise the detection of *Mycobacterium bovis* infected animals (bTB) in cattle herds. Understanding the relationships between herd and animal risk factors and IFN-γ test results is critical to enable the development and evaluation of policy measures on how best to use the test. In this study, we set out to characterise Irish herds with IFN-γ test positive animals in terms of herd size, number of SICTT reactors and number of IFN-γ positive tests, and to evaluate the IFN-γ test in terms of the test cut-off values. The results showed that larger herds with more SICTT reactors were likely to have more IFN-γ positives in the herd, and herds with an IFN-γ test positive animal that was also positive for bTB lesions at post-mortem had higher numbers of IFN-γ positive animals in the herd. Raising the cut-off values for the IFN-γ test only marginally decreased the combined sensitivity of the IFN-γ and the SICTT for diagnosis of bTB lesioned animals. The analysis has provided valuable information on the performance of the IFN-γ test as it is used under current bTB infection levels in Ireland.

Trends and predictors of large tuberculosis episodes in cattle herds in Ireland

Clegg, T.A.[1], Good, M.[2], Hayes, M.[3], Duignan, A.[3], McGrath, G.[1], More, S.J.[1]

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Frontiers in Veterinary Science 5, 86 (2018)

Persistence of bovine tuberculosis (bTB) in cattle is an important feature of *Mycobacterium bovis* infection, presenting either as herd recurrence or local persistence. One risk factor associated with the risk of recurrent episodes is the severity of a previous bTB episode (severity reflecting the number of bTB reactors identified during the episode). In this study, we have sought to identify predictors that can distinguish between small (less severe) and large (more severe) bTB episodes, and to describe nationally the severity of bTB episodes over time. The study included descriptive statistics of the proportion of episodes by severity from 2004 to 2015 and a case-control study. The case-control study population included all herds with at least one episode beginning in 2014 or 2015, with at least two full herd tests during the episode and a minimum herd-size of 60 animals. Case herds included study herds with at least 13 reactors whereas control herds had between 2 to 4 (inclusive) reactors during the first 2 tests of the episode. A logistic regression model was developed to identify risk factors associated with a large episode. Although there has been a general trend towards less severe herd bTB episodes in Ireland over time (2004–2015), the proportion of large episodes has remained relatively consistent. From the case-control study, the main predictors of a large episode were the year the episode started, increasing herd-size, previous exposure to bTB, increasing bTB incidence in the local area, an animal with a bTB lesion and a bTB episode in an associated herd. Herds that introduced more animals were more likely to have a smaller bTB

episode, reflecting the reduced risk of within-herd transmission when an episode was due to an introduced infected bTB animal. Some of the risk factors identified in this study such as reactors in previous bTB episodes, herds with an associated herd undergoing a bTB episode, herds in high incidence areas etc. may help to target future policy measures to specific herds or animals for additional surveillance measures. This information has important policy implications.

Do herds contiguous to controlled finishing units (feedlots) have an increased risk of experiencing a bovine tuberculosis breakdown?

Madden, J. et al.
UCD CVERA

This study will determine whether or not proximity to a feedlot is associated with increased or decreased risk of a bovine tuberculosis (bTB) breakdown. There are approximately 418 official feedlots currently restricted under the bTB eradication programme in Ireland and each are legally obliged to work under only one fragment of land. The aim of this study is to determine if herds contiguous to single fragment feedlots are associated with an increased or decreased risk of having bTB breakdowns.

Factory-based surveillance

The herd-level sensitivity of abattoir surveillance for bovine tuberculosis: simulating the effects of current and potentially modified meat inspection procedures in Irish cattle

Willeberg, P.W.[1], McAloon, C.G.[2], Houtsma, E.[3], Higgins, I.[3], Clegg, T.A.[3], More, S.J.[3]

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Frontiers in Veterinary Science 5, 82 (2018)

The European Food Safety Authority (EFSA) has published a series of opinions to assess the impact of changing from the current meat inspection procedures (CMI) to visual-only inspection (VOI) procedures. Concern has been raised that changes from CMI to VOI would adversely affect the effectiveness of surveillance for bovine tuberculosis (bTB) in EU member states, both for countries with and without official status of bTB freedom (OTF and non-OTF countries, respectively). This study was conducted to estimate the impact of a change from CMI to VOI in abattoirs on herd-level detection sensitivity in Ireland, a non-OTF country. Using national Irish data, we identified all herds that sold at least one animal to slaughter during 2010–12 whilst unrestricted for bTB. For each of these herds, we calculated the number of cattle sent to slaughter whilst unrestricted, the number of factory lesion tests (FLT) that had been performed, and estimated the apparent within-herd prevalence (AP_{wh}). A FLT is a whole-herd test conducted in a herd following the confirmation of bTB in an animal at slaughter. We considered five different inspection scenarios, each based on meat inspection and bacteriology in series, including current meat inspection (CMI) and four visual-only inspection scenarios (VOI2, VOI3, VOI4, VOI5) with reducing inspection sensitivities. Separately for each inspection scenario, a simulation model was used to estimate the herd-level detection sensitivity and the number of bTB-herds (that is, herds that sent at least one animal detected with *M. bovis* to slaughter when unrestricted during 2010–12) that would and would not be detected. The simulated mean herd-level detection sensitivity estimates were 0.24 for CMI, and 0.16, 0.12, 0.10 and 0.08 for VOI2-5, assuming a 2-, 3-, 4- and 5-fold decrease, respectively, in the animal-level detection sensitivity of VOI relative to that of CMI. The estimated number of non-detected bTB-herds is substantial with CMI, and increases in the series of VOI scenarios with decreasing herd-level detection sensitivity. If VOI were introduced without alternative surveillance means to compensate for the decrease in animal-level inspection sensitivity, such changes might jeopardise bTB surveillance, control and eradication programmes in cattle herds of non-OTF countries, including Ireland.

Supporting studies

Genetics, milk production

Simultaneous measurement of antigen-induced CXCL10 and IFN-γ enhances test sensitivity for bovine TB detection in cattle

Coad, M.[1], Doyle, M.[2], Steinbach, S.[1], Gormley, E.[2], Vordermeier, M.[1], Jones, G.[1]

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Veterinary Microbiology 230, 1-6 (2019)

Bovine tuberculosis (BTB) is a disease of economic and zoonotic importance caused mainly by *Mycobacterium bovis*. In addition to the tuberculin skin test, an interferon-gamma (IFN-γ) release assay (IGRA) blood test has been incorporated in the BTB control programs of numerous countries as an ancillary test to the skin test. A potential disadvantage of the IGRA assay is that it relies solely on the measurement of a single readout (i.e. IFN-γ) for the detection of BTB. In this study we have assessed the practical use of CXCL10 as an additional biomarker for the diagnosis of BTB in the setting of the current testing approach alongside IGRA. To do so, we have assessed both IFN-γ and CXCL10 readouts in blood cultures from a variety of different BTB cattle groups stimulated with standard tuberculin reagents and also with more specific defined antigens (ESAT-6, CFP-10 and Rv3615c). When using a tuberculin based whole blood assay, CXCL10 alone could not substitute for IFN-γ as the analyte measured in the test without reducing the sensitivity of detecting BTB animals. However, when used as an additional test readout, CXCL10 identified BTB animals that failed to induce IFN-γ responses. When tested in non-infected animals, the use of the dual biomarker system had the potential to lower overall test specificity, however this could be overcome by raising the cut-off values for CXCL10 test positivity. Taken together, the results demonstrate that in particular settings, measurement of CXCL10 has the potential to complement the current use of IFN-γ in blood assays to maximise the detection of BTB.

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Raw milk cheese produced from *M. bovis* infected herds: What is the risk?

Collins, Á. et al.

DAFM & UCD CVERA

The recent rise in consumer demand for speciality cheeses, which are often produced using raw milk, and the persistence of *Mycobacterium bovis* in the national herd has highlighted the risk of zoonotic *M. bovis* (bTB) infection from consuming cheese produced from raw milk from bTB infected herds in Ireland. Currently, published data quantifying this risk is lacking. This study will develop a risk assessment method to estimate the risk of human bTB infection from consuming cheese produced from raw milk originating in bTB infected herds.

Evaluation of the methodological quality of studies of the performance of diagnostic tests for bovine tuberculosis using QUADAS adapted for the veterinary field

Downs, S.H.[1], More, S.J.[2], Goodchild, A.V.[1], Whelan, A.O.[1, 3], Abernethy, D.A.[4, 5], Broughan, J.M.[1], Cameron, A.[6], Cook, A.J.[1, 7], de la Rua-Domenech, R.[8], Greiner, M.[9], Gunn, J.[1], Nuñez-Garcia, J.[1], Rhodes, S.[1], Rolfe, S.[10], Sharp, M.[1], Upton, P.[1], Watson, E.[1, 11], Welsh, M.[12, 13], Woolliams, J.A.[14], Clifton-Hadley, R.S.[1], Parry, J.E.[1]

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Preventive Veterinary Medicine 153, 108-116 (2018)

There has been little assessment of the methodological quality of studies measuring the performance (sensitivity and/or specificity) of diagnostic tests for animal diseases. In a systematic review, 190 studies of tests for bovine tuberculosis (bTB) in cattle (published 1934–2009) were assessed by at least one of 18 reviewers using the QUADAS (Quality Assessment of Diagnostic Accuracy Studies) checklist adapted for animal disease tests. VETQUADAS (VQ) included items measuring clarity in reporting (n = 3), internal validity (n = 9) and external validity (n = 2). A similar pattern for compliance was observed in studies of different diagnostic test types. Compliance significantly improved with year of publication for all items measuring clarity in reporting and external validity but only improved in four of the nine items measuring internal validity ($p < 0.05$). 107 references, of which 83 had performance data eligible for inclusion in a meta-analysis were reviewed by two reviewers. In these references, agreement between reviewers' responses was 71% for compliance, 32% for unsure and 29% for non-compliance. Mean compliance with reporting items was 2, 5.2 for internal validity and 1.5 for external validity. The index test result was described in sufficient detail in 80.1% of studies and was interpreted without knowledge of the reference standard test result in only 33.1%. Loss to follow-up was adequately explained in only 31.1% of studies. The prevalence of deficiencies observed may be due to inadequate reporting but may also reflect lack of attention to methodological issues that could bias the results of diagnostic test performance estimates. QUADAS was a useful tool for assessing and comparing the quality of studies measuring the performance of diagnostic tests but might be improved further by including explicit assessment of population sampling strategy.

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Methodology and preliminary results of a systematic literature review of ante-mortem and post-mortem diagnostic tests for bovine tuberculosis

Downs, S.H.[1], Parry, J.E.[1], Upton, P.A.[1], Broughan, J.M.[1], Goodchild, A.V.[1], Nuñez-Garcia, J.[1], Greiner, M.[2], Abernethy, D.A.[3, 4], Cameron, A.R.[5], Cook, A.J.[1, 6], de la Rua-Domenech, R.[7], Gunn, J.[1], Pritchard, E.[1], Rhodes, S.[1], Rolfe, S.[8], Sharp, M.[1], Vordermeier, H.M.[1], Watson, E.[1, 9], Welsh, M.[10, 11], Whelan, A.O.[1, 12], Woolliams, J.A.[13], More, S.J.[14], Clifton-Hadley, R.S.[1]

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Preventive Veterinary Medicine 153, 117-126 (2018)

A systematic review was conducted to identify studies with data for statistical meta-analyses of sensitivity (Se) and specificity (Sp) of ante-mortem and post-mortem diagnostic tests for bovine tuberculosis (bTB) in cattle. Members of a working group (WG) developed and tested search criteria and developed a standardised two-stage review process, to identify primary studies with numerator and denominator data for test performance and an agreed range of covariate data. No limits were applied to year, language, region or type of test in initial searches of electronic databases. In stage 1, titles and available abstracts were reviewed. References that complied with stage 1 selection criteria were reviewed in entirety and agreed data were extracted from references that complied with stage 2 selection criteria. At stage 1, 9782 references were reviewed and 261 (2.6%) passed through to stage 2 where 215 English language references were each randomly allocated to two of 18 WG reviewers and 46 references in other languages were allocated to native speakers. Agreement regarding eligibility between reviewers of the same reference at stage 2 was moderate (Kappa statistic = 0.51) and a resolution procedure was conducted. Only 119 references (published 1934–2009) were identified with eligible performance estimates for one or more of 14 different diagnostic test types; despite a comprehensive search strategy and the global impact of bTB. Searches of electronic databases for diagnostic test performance data were found to be nonspecific with regard to identifying references with diagnostic test Se or Sp data. Guidelines for the content of abstracts to research papers reporting diagnostic test performance are presented. The results of meta-analyses of the sensitivity and specificity of the tests, and of an evaluation of the methodological quality of the source references, are presented in accompanying papers (Nuñez-Garcia et al., 2017; Downs et al., 2017).

Cross reactive immune responses in cattle arising from exposure to *Mycobacterium bovis* and non-tuberculous mycobacteria

Jenkins, A.O.[1, 4], Gormley, E.[2], Gcebe, N.[3], Fosgate, G.T.[5], Conan, A.[6], Aagaard, C.[7], Michel, A.L.[4], Rutten, V.P.M.G.[1]

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Preventive Veterinary Medicine 152, 16-22. (2018)

Accurate diagnosis of tuberculosis in cattle may be compromised in areas where there are high rates of exposure to environmental/non-tuberculous mycobacteria (NTM). This cross reaction of immune responses to *Mycobacterium bovis* antigens shared with NTMs can result in reduced specificity of commonly used diagnostic tests including tuberculin skin tests and the interferon gamma assay (IFN-γ). In this study we assessed the cross-reactive immune responses of *M. bovis* (infected) and NTM exposed animals to *M. bovis* and *M. avium* tuberculin, the ESAT6/CFP10 cocktail antigen, tuberculin derived from cultures of selected NTMs, and a panel of recombinant mycobacterium tuberculosis complex (MTBC) antigens sharing homology with orthologues in NTM. Gamma interferon (IFN-γ) responses were measured in whole blood cultures using the IFN-γ assay and the IFN-γ elispot assay on purified peripheral blood mononuclear cells (PBMC). We observed the expected strong IFN-γ response to PPD-B in the *M. bovis* infected animals that distinguished this group from non-infected NTM exposed cattle. The IFN-γ responses to PPD-N (*M. nonchromogenicum*), were relatively high in both infected and non-infected NTM exposed cattle, but were not significantly different to classify the true infection status of each group. The results indicated that the cross-reactive responses to PPD-B and/or PPD-A with PPD-N, likely arose from prior exposure to environmental non-tuberculous mycobacteria. The IFN-γ immune responses to the 10 R-Mag measured by the IFN-γ elispot assay revealed that three of the selected antigens, Rv3615 (ESpC), Rv0287 (esxG) and the ESAT6/CFP10, were immunogenic in the infected cattle, and distinguished the infected cattle from the non-infected NTM exposed animals. The combined data of PPDs and R-Mags derived from NTM mycobacteria may prove useful in future development of novel bTB diagnostic tests.

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Spatial representation of the specificity of the SICCT test in cattle herds in Ireland

McGrath, G. et al.
UCD CVERA

This study will explore the spatial and temporal distribution of the specificity of the Single Intradermal Comparative Cervical Skin (SICCT) test in cattle herds across Ireland using Geographical Information Systems and statistical analysis. This project aims to test the commonly believed idea that some areas in Ireland are prone to having positive SICCT tests caused by non-Tuberculous mycobacteria. If these areas are detectable, herds occurring within them could be flagged helping local Veterinary Inspectors with interpretation of herds with persistent single reactor tests.

Comparative ‘omics analyses differentiate *Mycobacterium tuberculosis* and *Mycobacterium bovis* and reveal distinct macrophage responses to infection with the human and bovine tubercle bacilli

Malone, K.M.[1, 7], Rue-Albrecht, K.[1, 2, 8], Magee, D.A.[2], Conlon, K.[1], Schubert, O.T.[3, 9], Nalpas, N.C.[2, 10], Browne, J.A.[2], Smyth, A.[1], Gormley, E.[1], Aebersold, R.[3], MacHugh, D.E.[2, 4], Gordon, S.V.1, [4, 5, 6]

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Microbial Genomics 2018, 4 (2018)

Members of the *Mycobacterium tuberculosis* complex (MTBC) are the causative agents of tuberculosis in a range of mammals, including humans. A key feature of MTBC pathogens is their high degree of genetic identity yet distinct host tropism. Notably, while *Mycobacterium bovis* is highly virulent and pathogenic for cattle, the human pathogen *M. tuberculosis* is attenuated in cattle. Previous research also suggests that host preference amongst MTBC members has a basis in host innate immune responses. To explore MTBC host tropism, we present in-depth profiling of the MTBC reference strains *M. bovis* AF2122/97 and *M. tuberculosis* H37Rv at both the global transcriptional and the translational level via RNA-sequencing and SWATH MS. Furthermore, a bovine alveolar macrophage infection time course model was used to investigate the shared and divergent host transcriptomic response to infection with *M. tuberculosis* H37Rv or *M. bovis* AF2122/97. Significant differential expression of virulence-associated pathways between the two bacilli was revealed, including the ESX-1 secretion system. A divergent transcriptional response was observed between *M. tuberculosis* H37Rv and *M. bovis* AF2122/97 infection of bovine alveolar macrophages, in particular cytosolic DNA-sensing pathways at 48 h post-infection, and highlights a distinct engagement of *M. bovis* with the bovine innate immune system. The work presented here therefore provides a basis for the identification of host innate immune mechanisms subverted by virulent host-adapted mycobacteria to promote their survival during the early stages of infection.

Meta-analyses of the sensitivity and specificity of ante-mortem and post-mortem diagnostic tests for bovine tuberculosis in the UK and Ireland

Nuñez-Garcia, J.[1], Downs, S.H.[1], Parry, J.E.[1], Abernethy, D.A.[2, 3], Broughan, J.M.[1], Cameron, A.R.[4], Cook, A.J.[1, 5], de la Rua-Domenech, R.[6], Goodchild, A.V.[1], Gunn, J.[1], More, S.J.[7], Rhodes, S.[1], Rolfe, S.[8], Sharp, M.[1], Upton, P.A.[1], Vordermeier, H.M.[1], Watson, E.[1, 9], Welsh, M.[10, 11], Whelan, A.O.[1, 12], Woolliams, J.A.[13], Clifton-Hadley, R.S.[1], Greiner, M.[14]

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Preventive Veterinary Medicine 153, 94-107 (2018)

Bovine tuberculosis (bTB) in cattle is a global health problem and eradication of the disease requires accurate estimates of diagnostic test performance to optimize their efficiency. The objective of this study was, through statistical meta-analyses, to obtain estimates of sensitivity (Se) and specificity (Sp), for 14 different ante-mortem and post-mortem diagnostic tests for bTB in cattle. Using data from a systematic review of the scientific literature (published 1934–2009) diagnostic Se and Sp were estimated using Bayesian logistic regression models adjusting for confounding factors. Random effect terms were used to account for unexplained heterogeneity. Parameters in the models were implemented using Markov Chain Monte Carlo (MCMC), and posterior distributions for the diagnostic parameters with adjustment for covariates (confounding factors) were obtained using the inverse logit function. Estimates for Se and/or Sp of the tuberculin skin tests and the IFN-γ blood test were compared with estimates published 2010–2015. Median Se for the single intradermal comparative cervical tuberculin skin (SICCT) test (standard interpretation) was 0.50 and Bayesian credible intervals (CrI) were wide (95% CrI 0.26, 0.78). Median Sp for the SICCT test was 1.00 (95% CrI 0.99, 1.00). Estimates for the IFN-γ blood test Bovine Purified Protein Derivative (PPD)-Avian PPD and Early Secreted Antigen target 6 and Culture Filtrate Protein 10 (ESAT-6/CFP10) ESAT6/CFP10 were 0.67 (95% CrI 0.49, 0.82) and 0.78 (95% CrI 0.60, 0.90) respectively for Se, and 0.98 (95% CrI 0.96, 0.99) and 0.99 (95% CrI 0.99, 1.00) for Sp. The study provides an overview of the accuracy of a range of contemporary diagnostic tests for bTB in cattle. Better understanding of diagnostic test performance is essential for the design of effective control strategies and their evaluation.

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Improved understanding of ecology and TB epidemiology

Badger ecology

Push and pull factors driving movement in a social mammal: context dependent behavioral plasticity at the landscape scale

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Current Zoology 65, 517-525 (2019)

Understanding how key parameters (e.g., density, range-size, and configuration) can affect animal movement remains a major goal of population ecology. This is particularly important for wildlife disease hosts, such as the European badger *Meles meles*, a reservoir of *Mycobacterium bovis*. Here we show how movements of 463 individuals among 223 inferred group territories across 755 km^2 in Ireland were affected by sex, age, past-movement history, group composition, and group size index from 2009 to 2012. Females exhibited a greater probability of moving into groups with a male-biased composition, but male movements into groups were not associated with group composition. Male badgers were, however, more likely to make visits into territories than females. Animals that had immigrated into a territory previously were more likely to emigrate in the future. Animals exhibiting such "itinerant" movement patterns were more likely to belong to younger age classes. Inter-territorial movement propensity was negatively associated with group size, indicating that larger groups were more stable and less attractive (or permeable) to immigrants. Across the landscape, there was substantial variation in inferred territory-size and movement dynamics, which was related to group size. This represents behavioral plasticity previously only reported at the scale of the species' biogeographical range. Our results highlight how a "one-size-fits-all" explanation of badger movement is likely to fail under varying ecological contexts and scales, with implications for bovine tuberculosis management.

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Wild animal tuberculosis: stakeholder value systems and management of disease

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Frontiers in Veterinary Sciences 5, 327 (2018)

When human health is put at risk from the transmission of animal diseases, the options for intervention often require input from stakeholders whose differing values systems contribute to decisions on disease management. Animal tuberculosis (TB), caused principally by *Mycobacterium bovis* is an archetypical zoonotic pathogen in that it can be transmitted from animals to humans and *vice versa*. Although elimination of zoonotic transmission of TB to humans is frequently promoted as the *raison d'être* for TB management in livestock, in many countries the control strategies are more likely based on minimizing the impact of sustained infection on the agricultural industry. Where wild animals are implicated in the epidemiology of the disease, the options for control and eradication can require involvement of additional stakeholder groups. Conflict can arise when different monetary and/or societal values are assigned to the affected animals. This may impose practical and ethical dilemmas for decision makers where one or more species of wild animal is seen by some stakeholders to have a greater value than the affected livestock. Here we assess the role of stakeholder values in influencing TB eradication strategies in a number of countries including Ireland, the UK, the USA, Spain, France, Australia, New Zealand and South Africa. What it reveals is that the level of stakeholder involvement increases with the complexity of the epidemiology, and that similar groups of stakeholders may agree to a set of control and eradication measures in one region only to disagree with applying the same measures in another. The level of consensus depends on the considerations of the reservoir status of the infected host, the societal values assigned to each species, the type of interventions proposed, ethical issues raised by culling of sentient wild animals, and the economic cost benefit effectiveness of dealing with the problem in one or more species over a long time frame. While there is a societal benefit from controlling TB, the means to achieve this requires identification and long-term engagement with all key stakeholders in order to reach agreement on ethical frameworks that prioritize and justify control options, particularly where culling of wild animals is concerned.

Environmental dust inhalation in the European badger (*Meles meles*): Systemic distribution of silica-laden macrophages, pathological changes, and association with *Mycobacterium bovis* infection status

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PLoS One 13, e0190230 (2018)

Chronic inhalation of crystalline silica and silicates may lead to severe lung disease in humans, termed silicosis. The disease is an occupational health concern in miners and related professions worldwide. Silicosis is also a strong risk factor for tuberculosis in humans. Due to its subterranean lifestyle, the European badger (*Meles meles*) is continuously exposed to environmental dust, while this species is also susceptible to tuberculosis, caused by *Mycobacterium bovis*. To date, a thorough investigation of mineral dust retention and its possible implication as a risk factor for mycobacterial infection in badgers has not been performed. The aims of this retrospective histological study were (1) to describe the systemic tissue distribution of silica-laden macrophages (SLMs) in badgers; (2) to compare the amount of SLMs in tissues of badgers of differing *M. bovis* infection status, pulmonary SLM burden and age; and (3) to assess whether inflammation was associated with SLMs. We assessed lung, lymph nodes, liver and spleen of 60 wild-caught badgers of known *M. bovis* infection status for the presence of SLMs using polarizing light microscopy. SLMs were consistently present within the lungs and were widely distributed throughout the lymphatic system. No inflammatory reaction to SLMs, as occurs in human silicosis, was observed in any tissue. Distribution and amount of SLMs were similar between *M. bovis* positive and negative badgers, and we were not able to show an association between the amount of SLMs and *M. bovis* infection status. The amount of SLMs within intra- and extrathoracic lymph nodes was positively associated with the amount of pulmonary SLMs, and with age. This is the first report of substantial and systemic tissue retention of mineral dust particles in a mammalian species lacking associated chronic inflammation (i.e. silicosis). We further highlight different pathogenetic mechanisms underlying silicosis and benign SLM accumulations following siliceous dust inhalation.

Monitoring European badger (*Meles meles*) reproduction under evolving bovine tuberculosis management in Ireland

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European Journal of Wildlife Research 65, 97 (2019)

Wildlife disease management often relies on altering population abundance and density to reduce the susceptible host population. Understanding the vital rates and ecology that influence wildlife population dynamics is important for assessing the outcomes of management policies. European badgers (*Meles meles*) in Ireland have historically been managed for bovine tuberculosis (TB) using culling, but are now being vaccinated instead. We used data from 6847 badgers submitted for postmortem examination from 2016 to 2018 to inform population monitoring of badgers under this management change. Female reproductive status varied strongly by month, and a considerable proportion (25–40%) of females had evidence of premature cessation of lactation. Teat lengths may offer a crude guideline for rapid antemortem assessment of probable reproductive status. Body weight for males and females declined throughout the capture period, and we report reference ranges for normal male and female body weight during each month. Increasing body weight was associated with an increased odds of pregnancy (OR 2.52, 95% CI 2.20–2.93, $p < 0.001$). Prior capturing at the sett where a badger was captured did not affect the odds of pregnancy (OR = 0.99, 95% CI 0.96–1.03, $p = 0.77$) or influence litter size ($\beta = -0.0012$, SE = 0.014, $p = 0.93$). Assessing changes in badger reproduction will ensure that management is adapted for a badger population likely to expand and contribute to a successful TB eradication program in Ireland.

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Infection control strategies

Gamma-interferon (IFN-γ) blood testing and research

The gamma-interferon (IFN-γ) assay is used as a tool by ERAD to assist in the eradication of bovine tuberculosis from the national herd. In addition to the UCD laboratory, the Cork Blood Testing Laboratory (BTL) has recently commenced full IFN-γ testing in infected herds from the southern regions of the country. The Sligo Regional Veterinary Laboratory continues carrying out the first (stimulation) stage of the assay, with blood plasmas transported to UCD for the second stage ELISA step. In the period 2018-2019, approx. 88,000 blood samples were submitted to the laboratory for IFN-γ testing. Along with the Cork BTL lab submissions (approx 25,000 samples), this represents a substantial increase compared with submission numbers for the previous two years (91,000 samples). The samples submitted for IFN-γ test currently originate mainly from:

- bovine reactor re-test herds, where the IFN-γ test is used to diagnose infected animals that are missed by the SICTT (false negatives).
- SICTT reactor animals where the IFN-γ test is used to confirm the exposure status of SICTT positive animals. This testing is conducted as part of the ERAD Quality Assurance programme.

The laboratory continues to conduct research with a view to improving the performance of the assay under Irish conditions. A number of key studies have been completed and published in the past two years.

Characteristics of herds tested for IFN-γ

Along with CVERA, we investigated the relationships between herd and animal risk factors and IFN-γ test results, as this is critical to enable the development and evaluation of policy measures on how best to use the test. In this study, we looked at Irish herds with IFN-γ test positive animals in terms of herd size, number of SICTT reactors and number of IFN-γ positive tests, and to evaluate the IFN-γ test in terms of the test cut-off values. The results showed that larger herds with more SICTT reactors were likely to have more IFN-γ positives in the herd, and herds with an IFN-γ test positive animal that was also positive for bTB lesions at post-mortem had higher numbers of IFN-γ positive animals in the herd. Raising the cut-off values for the IFN-γ test only marginally decreased the combined sensitivity of the IFN-γ and the SICTT for diagnosis of bTB lesioned animals. The analysis has provided valuable information on the performance of the IFN-γ test as it is used under current bTB infection levels in Ireland.

Investigation of cross reactive immune responses in cattle arising from exposure to **Mycobacterium bovis** *and non-tuberculous mycobacteria*

Accurate diagnosis of tuberculosis in cattle may be compromised in areas where there are high rates of exposure to environmental /non-tuberculous mycobacteria (NTM). This cross reaction of immune responses to *Mycobacterium bovis* antigens shared with NTMs can result in reduced specificity of commonly used diagnostic tests including tuberculin skin tests and the interferon gamma assay (IFN-γ). In this study we assessed the cross-reactive immune responses of *M. bovis* (infected) and NTM exposed animals to *M. bovis* and *M. avium* tuberculin, the ESAT6/CFP10 cocktail antigen, tuberculin derived from cultures of selected NTMs, and a panel of recombinant mycobacterium tuberculosis complex (MTBC) antigens sharing homology with NTM. As expected, we observed a strong IFN-γ response to PPD-B in the *M. bovis* infected animals that distinguished this group from non-infected NTM exposed cattle. The responses to PPD-V derived from *M. vaccae* could also discriminate between both groups of animals. The IFN-γ responses to PPD-N (*M. nonchromogenicum*), were relatively high in both infected and non-infected NTM exposed cattle, but were not significantly different to classify the true infection status of each group. The results indicated that the cross-reactive responses to PPD-B and/or PPD-A with PPD-N likely arose from prior exposure to environmental non-tuberculous mycobacteria.

Simultaneous measurement of antigen-induced CXCL10 and IFN-γ enhances test sensitivity for bovine TB detection in cattle

In previous work we investigated additional biomarkers of immune activation with a view to improving the performance of bTB diagnostic assays. Among these, interferon gamma-induced protein 10 (IP-10, also known as CXCL10) has proven particularly noteworthy. We demonstrated that the release of CXCL10 was a potentially valuable biomarker of *M. bovis* infection in cattle and measurement of this cytokine might serve to improve the diagnostic sensitivity of whole blood stimulation. In a follow up study, we provided samples and knowledge to colleagues at APHA-UK as part of a wider project to determine if measurement of antigen-induced CXCL10 and IFN-γ enhanced bTB diagnostic test sensitivity. In the whole blood assay, CXCL10 alone could not substitute for IFN-γ as measured in the test without reducing the sensitivity of detecting bTB animals. However, when used as an additional test readout, CXCL10 identified BTB animals that failed to induce IFN-γ responses. Taken together, the results demonstrate that in particular settings, measurement of CXCL10 has the potential to complement the current use of IFN-γ in blood assays to maximise the detection of bTB.

Additional IFN-γ laboratory research

The laboratory is engaged in studies to identify additional cytokine biomarkers of bTB infection and to understand the complex interplay between the expression of cytokines that impact on the levels of IFN-γ produced in the assay. We continue to carry out research on estimating the potency of tuberculin using the IFN-γ assay. The lab is also engaged in active research with groups based at UCD and elsewhere to use advanced transcriptomic tests to better understand the specific immune responses to infection with tuberculosis.

The badger vaccine development programme

Measurement of seroconversion in badgers vaccinated with BCG vaccine strain Sofia by the intra-muscular route

For historical reasons there are several different strains of BCG used worldwide and up until four years ago the BCG Danish strain, manufactured in Denmark, was the only commercially licensed BCG vaccine for use in the EU and the vaccine of choice for delivery to badgers in Ireland and UK. However, production of BCG Danish ceased for a number of years due to a commercial takeover and issues relating to product manufacture. DAFM gained access to another widely used BCG strain named Sofia. This is a UNICEF approved vaccine strain used widely in humans in the developing world. Blood from animals that have been vaccinated with different BCG strains (including the Danish strain) do not generally respond in the blood test. However, the situation is not known for the BCG Sofia vaccine. Thus, there is a possibility that animals vaccinated with BCG Sofia will respond in the blood test for TB. We recently conducted a study to determine if seroconversion occurred in the blood of badgers vaccinated with BCG vaccine strain Sofia by the intramuscular route. A group of captive badgers was vaccinated with BCG Sofia by the intramuscular route. Blood samples were collected pre- and post-vaccination to see if there is a change in antibody status over time. As boosting with a vaccine is often associated with increased antibody production, the badgers were given a booster vaccine at 12 weeks and re-vaccinated at 52 weeks to determine the impact of boosting on blood responses. Preliminary analysis of data suggests that repeat vaccination of badgers with BCG Sofia has the potential to compromise the only commercially available blood test for TB infection in badgers. The benefit of the study is that it has provided novel information to make recommendations to DAFM on specific strategies for deployment of BCG vaccine to badgers as part of the national vaccination programme.

Development of novel badger immunodiagnostics: New serological platform for detecting antibodies against* Mycobacterium tuberculosis *complex in European badgers

In addition to the vaccination research programme, the UCD laboratory also assisted in the development and validation of new serological tests for diagnosis of tuberculosis in badgers in collaboration with APHA, and a consortium lead by VISAVET Health Surveillance Centre, Universidad Complutense de Madrid. We contributed to the evaluation of two new ELISA platforms for recognition of the P22 multiprotein complex derived from the purified protein derivative (PPD) of *M. bovis*. The two ELISA tests showed estimated sensitivity levels of 74%-82% in experimentally and naturally infected badgers with specificities ranging from 75% to 100% depending on the badger population tested. These ELISAs based on the P22 multi-antigen potentially provide a sensitive and specific test platform for improved tuberculosis surveillance in badgers. We are also providing samples and expertise to joint Ireland - UK studies to validate a number of novel diagnostic tests.

Progress towards a badger vaccine

Quantification of *Mycobacterium bovis* transmission in a badger vaccine field trial

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Preventive Veterinary Medicine 149, 29-37 (2018)

In the UK and Ireland, Bacille Calmette-Guérin (BCG) vaccination of badgers has been suggested as one of a number of strategies to control or even eradicate *Mycobacterium bovis* infection in badgers. In this manuscript, we present the results of a badger field trial conducted in Ireland and discuss how the novel trial design and analytical methods allowed the effects of vaccination on protection against infection and, more importantly, on transmission to be estimated. The trial area was divided into three zones North to South (A, B and C) where vaccination coverages of 0, 50 and 100%, respectively, were applied. Badgers were trapped over a 4 year period. Badgers were assigned to either placebo or vaccine treatment, with treatment allocation occurring randomly in zone B. Blood samples were collected at each capture, and serology was performed in these samples using a chemiluminescent multiplex ELISA system (Enfer test). The analysis aimed to compare new infections occurring in non-infected non-vaccinated badgers to those in non-infected vaccinated ones, while accounting for the zone in which the badger was trapped and the infection pressure to which this individual badger was exposed. In total, 440 records on subsequent trappings of individual non-infected badgers were available for analysis. Over the study period, 55 new infections occurred in non-vaccinated (out of 239 = 23.0%) and 40 in vaccinated (out of 201 = 19.9%) badgers. A Generalized Linear Model (GLM) with a cloglog link function was used for analysis. Statistical analysis showed that susceptibility to natural exposure with *M. bovis* was reduced in vaccinated compared to placebo treated badgers: vaccine efficacy for susceptibility, VEs, was 59% (95% CI = 6.5%–82%). However, a complete lack of effect from BCG vaccination on the infectivity of vaccinated badgers was observed, i.e. vaccine efficacy for infectiousness (VEI) was 0%. Further, the basic reproduction ratio as a function of vaccination coverage (p) (i.e. R(p)) was estimated. Given that the prevalence of *M. bovis* infection in badgers in endemic areas in Ireland is approximately 18%, we estimated the reproduction ratio in the unvaccinated population as R(0) = 1.22. Because VES was now known, the reproduction ratio for a fully vaccinated population was estimated as R(1) = 0.50. These results imply that with vaccination coverage in badgers exceeding 30%, eradication of *M. bovis* in badgers in Ireland is feasible, provided that the current control measures also remain in place.

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Characterising transmission of *Mycobacterium bovis* in a multi-host system

Aznar, I. et al.

UCD CVERA, DAFM & Wageningen Institute of Animal Sciences, Wageningen University & Research, Wageningen, The Netherlands

This is the final chapter of Inma Aznar's PhD, which was entitled 'Infection dynamics and effective control strategies of tuberculosis in badgers and cattle in Ireland'. The final chapter is particular important as it considers the practical implications of insights gained from a quantitative assessment of *M. bovis* transmission in the cattle-badger system in Ireland. The aim of this work was to develop new algorithms to allow quantification of transmission originating from each of the species (next generation matrices; NGM) and the reproduction ratio (R) for the system based on readily available data. The effect on R achieved by badger vaccination is estimated in all plausible transmission scenarios, and the impact of badger vaccination in addition to all current control strategies in Ireland is discussed.

Two host species transmission data analysis and modelling to calculate risk maps for bovine TB during eradication by badger vaccination in the Republic of Ireland (ROI)

Barber, A.[1, 2], Chang, Y.[1], et al.

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Previous work, conducted by Aznar et al., investigated infection dynamics and effective control strategies of bTB in cattle and badgers in Ireland. A key finding of the work concerned the possibility that badger vaccination in addition to all current controls could successfully achieve eradication of *M. bovis* in the overall cattle-badger system in Ireland. These analyses were based on prevalence estimates in cattle and badgers averaged over the whole of the country. The aims of the current study are to i) quantify local transmission in the badger-cattle system (i.e. at a smaller spatial scale), identifying potential hotspots, and thereby possible difficulties in achieving eradication, ii) evaluate the effectiveness of the badger vaccination strategy in terms of its ability to sufficiently reduce transmission in the badger-cattle system in combination with current control measures. Risk-maps will be generated to provide insights on where transmission cannot be sustained or is likely to persist and iii) develop a dynamical model to disentangle the relative importance of each transmission mechanism (i.e direct transmission, indirect transmission via the environment and cattle movement) in bTB spread and estimate the cost-effectiveness of interventions on different transmission routes.

Pathogenesis of *Mycobacterium bovis* infection: the badger model as a paradigm for understanding tuberculosis in animals

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Frontiers in Veterinary Science 4, 247 (2018)

Tuberculosis in animals is caused principally by infection with *Mycobacterium bovis* and the potential for transmission of infection to humans is often the fundamental driver for surveillance of disease in livestock and wild animals. However, with such a vast array of species susceptible to infection, it is often extremely difficult to gain a detailed understanding of the pathogenesis of infection – a key component of the epidemiology in all affected species. This is important because the development of disease control strategies in animals is determined chiefly by an understanding of the epidemiology of the disease. The most revealing data from which to formulate theories on pathogenesis are that observed in susceptible hosts infected by natural transmission. These data are gathered from detailed studies of the distribution of gross and histological lesions, and the presence and distribution of infection as determined by highly sensitive bacteriology procedures. The information can also be used to establish the baseline for evaluating experimental model systems.
The European badger (*Meles meles*) is one of a very small number of wild animal hosts where detailed knowledge of the pathogenesis of *M. bovis* infection has been generated from observations in natural-infected animals. By drawing parallels from other animal species, an experimental badger infection model has also been established where infection of the lower respiratory tract mimics infection and the disease observed in natural-infected badgers. This has facilitated the development of diagnostic tests and testing of vaccines that have the potential to control the disease in badgers. In this review, we highlight the fundamental principles of how detailed knowledge of pathogenesis can be used to evaluate specific intervention strategies, and how the badger model may be a paradigm for understanding pathogenesis of tuberculosis in any affected wild animal species.

New serological platform for detecting antibodies against *Mycobacterium tuberculosis* complex in European badgers

Infantes-Lorenzo, J.A.[1], Dave, D.[2], Moreno, I.[3], Anderson, P.[2], Lesellier, S.[2], Gormley, E.[4], Dominguez, L.[1], Balseiro, A.[5], Gortázar, C.[6], Dominguez, M.[3], Salguero, F.J.[7]

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Veterinary Medicine and Science 5, 61–69 (2019)

European badgers (*Meles meles*) have been identified as wildlife reservoirs for *Mycobacterium bovis* in the UK and Ireland, and may also have a role in the epidemiology of animal tuberculosis in other European regions. Thus, detection of *M. bovis*-infected badgers may be required for the purposes of surveillance and monitoring of disease levels in infected populations. Current serological assays to detect *M. bovis* infection in live badgers, while rapid and inexpensive, show limited diagnostic sensitivity. Here we describe and evaluate new ELISA platforms for the recognition of the P22 multiprotein complex derived from the purified protein derivative (PPD) of *M. bovis*. The recognition of IgG against

P22 multiprotein complex derived from PPD-B was tested by ELISA in the serum of badgers from the UK, Ireland and Spain. TB infection in the badgers was indicated by the presence of *M. bovis* in tissues by culture and histology at post-mortem examination and TB-free status was established by repeated negativity in the interferon γ release assay (IGRA). In experimentally infected badgers, humoral antibody responses against P22 developed within 45 days post-infection. The ELISA tests showed estimated sensitivity levels of 74–82% in experimentally and naturally infected badgers with specificities ranging from 75% to 100% depending on the badger population tested. The P22 multi-antigen based ELISAs provide a sensitive and specific test platform for improved tuberculosis surveillance in badgers.

Investigation into the genetic diversity in toll-like receptors 2 and 4 in the European badger *Meles meles*

Whiteoak, A.M.[1], Ideozu, J.[1], Alkathiry, H.[1], Tomlinson, A.J.[2], Delahay, R.J.[2], Cowen, S.[3], Mullineaux, E.[3], Gormley, E.[4], Birtles, R.J.[1], Lun, Z.R.[1, 5, 6], Hide, G.[1, 6]

[1] Ecosystems and Environment Research Centre, School of Environment and Life Sciences, University of Salford, England, [2] National Wildlife Management Centre, Animal and Plant Health Agency, Woodchester Park, Gloucestershire, England, [3] Secret World Wildlife Rescue, New Road, East Huntspill, Highbridge, England, [4] UCD School of Veterinary Medicine, [5] State Key Laboratory of Biocontrol, School of Life Sciences, Key Laboratory of Tropical Diseases and Control of the Ministry of Education, Zhongshan Medical School, Sun Yat-Sen University, Guangzhou, PR China, [6] Biomedical Research Centre, School of Environment and Life Sciences, University of Salford, England

Research in Veterinary Science 119, 228-231 (2018)

The Toll-like receptor (TLR) genes are a conserved family of genes central to the innate immune response to pathogen infection. They encode receptor proteins, recognise pathogen associated molecular patterns (PAMPs) and trigger initial immune responses. In some host-pathogen systems, it is reported that genetic differences, such as single nucleotide polymorphisms (SNPs), associate with disease resistance or susceptibility. Little is known about TLR gene diversity in the European badger (*Meles meles*). We collected DNA from UK badgers, carried out PCR amplification of the badger TLR2 gene and exon 3 of TLR4 and determined DNA sequences for individual badgers for TLR2 (n = 61) and TLR4 exon 3 (n = 59). No polymorphism was observed in TLR4. Three TLR2 amino acid haplotype variants were found. Ninety five percent of badgers were homozygous for one common haplotype (H1), the remaining three badgers had genotypes H1/H3, H1/H2 and H2/H2. By broad comparison with other species, diversity in TLR genes in badgers seems low. This could be due to a relatively localised sampling or inherent low genetic diversity. Further studies are required to assess the generality of the low observed diversity and the relevance to the immunological status of badgers.

Reprinted from Research in Veterinary Science, 119, *Whiteoak, Investigation into the genetic diversity in toll-like receptors 2 and 4 in the European badger* Meles meles, *228-231, Copyright 2018, with permission from Elsevier.*

Whole Genome Sequencing (WGS)

Comparative analysis of *M. bovis* in Britain and Ireland using phylodynamic approach - Whole Genome Sequencing (WGS) of *M. bovis* in badgers, cattle and deer

Crispell, J. et al.
UCD School of Veterinary Medicine

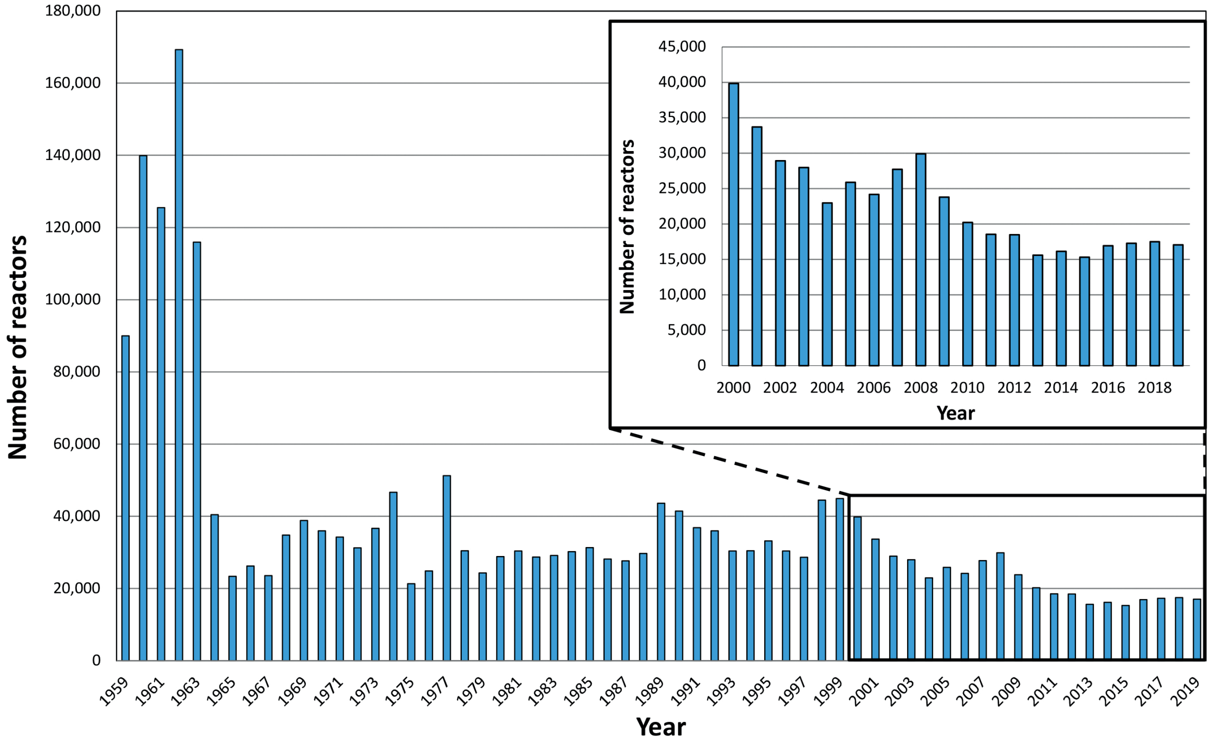
This study will explore the phylogeny of *M. bovis* across species in Co. Wicklow in the Republic of Ireland using WGS. The study aims to determine the occurrence of transmission of *M. bovis* between multiple species in Co. Wicklow and to develop appropriate methodologies for using WGS as an additional in the eradication programme.

Whole Genome Sequencing (WGS) analysis of *M. bovis* in a bTB cluster in Co. Monaghan

Crispell, J. et al.
UCD School of Veterinary Medicine

This study will utilise WGS to identify whether badgers and cattle in Co. Monaghan share common strains of *M. bovis*. Techniques will be refined to establish WGS methodologies for use as a tool in epidemiological investigations. Strains identified during this study will be included in a national database of *M. bovis* genetic sequences.

The national programme



The number of TB reactors detected in Ireland each year between 1959 and 2019

The bovine tuberculosis cluster in north County Sligo during 2014-16

Doyle, R.[1], Clegg, T.A.[2], McGrath, G.[2], Tratalos, J.[2], Barrett, D.[1], Lee, A.[3], More, S.J.[2]

[1] DAFM, [2] UCD CVERA, [3] Cyberport, Pokfulam, Hong Kong Island, Hong Kong

Irish Veterinary Journal 71, 24 (2018)

Bovine tuberculosis (bTB, caused by infection with *Mycobacterium bovis*) is endemic in the Irish cattle population, and the subject of a national eradication programme since the late 1950s. During 2014, a substantial area-level bTB outbreak developing in north County Sligo, necessitating the need for an enhanced response. This paper describes this outbreak, the response that was undertaken and some lessons learned. In the north Sligo area between 2014 and 2016, 23 (31.9%) of restricted herds had 4 or more reactors to the single intradermal comparative tuberculin test (SICTT)/animals with bTB lesions disclosed during the restriction, and the majority (55.5%) of test-positive animals were identified as standard reactors to the SICTT. The herds restricted during 2014–16 were typically larger than other herds in the study area and introduced more animals during 2013. *M. bovis* was also detected in local badgers, but not deer. This paper describes a substantial outbreak in north County Sligo over a 3-year period. A coordinated area-based approach was a key feature of the outbreak, and substantial resources were applied to bring the outbreak under control. No definitive source was identified, nor reasons why a substantial number of herds were infected over a relatively short period. A coordinated regional approach was taken, and a number of lessons were learned including the need for urgency, for a team-based approach, for a consistent message when dealing with the public, for an area-based approach, for a degree of flexibility for the breakdown manager, and for molecular tools to assist in answering key questions relating to the source and spread of *M. bovis* to many herds during this bTB outbreak.

The history of *in vivo* tuberculin testing in bovines: tuberculosis a "One Health" issue

Good, M.[1], Bakker, D.[2], Duignan, A.[3], Collins, D.M.[4]

[1] Independent researcher and private consultant, [2] Department of Animal Health, Faculty of Veterinary Medicine, Complutense University of Madrid, Madrid, Spain, [3] DAFM, [4] UCD CVERA

Frontiers in Veterinary Science 5, 59 (2018)

Tuberculosis (TB) is more than 3 million years old thriving in multiple species. Ancestral *Mycobacterium tuberculosis* gave rise to multiple strains including *Mycobacterium bovis* now distributed worldwide with zoonotic transmission happening in both directions between animals and humans. *M. bovis* in milk caused problems with a significant number of deaths in children under 5 years of age due largely to extrapulmonary TB. This risk was effectively mitigated with widespread milk pasteurization during the twentieth century, and fewer young children were lost to TB. Koch developed tuberculin in 1890 and recognizing the possibility of using tuberculin to detect infected animals the first tests were quickly developed. Bovine TB (bTB) control/eradication programmes followed in the late nineteenth century/early twentieth century. Many scientists collaborated and contributed to the development of tuberculin tests, to refining and optimizing the production and standardization of tuberculin and to determining test sensitivity and specificity using various methodologies and injection sites. The WHO, OIE, and EU have set legal standards for tuberculin production, potency assay performance, and intradermal tests for bovines. Now, those using tuberculin tests for bTB control/eradication programmes rarely see TB as a disease. Notwithstanding the launch of the first-ever roadmap to combat zoonotic TB, many wonder if bTB is actually a problem? Is there a better way of dealing with bTB? Might alternative skin test sites make the test "better" and easier to perform? Are all tuberculins used for testing equally good? Why have alternative "better" tests not been developed? This review was prompted by these types of questions. This article attempts to succinctly summarize the data in the literature from the late nineteenth century to date to show why TB, and zoonotic TB specifically, was and still is important as a "One Health" concern, and that the necessity to reduce the burden of zoonotic TB, to save lives and secure livelihoods is far too important to await the possible future development of novel diagnostic assays for livestock before renewing efforts to eliminate it. Consequently, it is highly probable that the tuberculin skin test will remain the screening test of choice for farmed livestock for the considerable future.

Further improvement in the control of bovine tuberculosis recurrence in Ireland

Houtsma, E.[1], Clegg, T.A.[1], Good, M.[2], More, S.J.[1]

[1] UCD CVERA, [2] Independent researcher and private consultant

Veterinary Record 183, 622 (2018)

Ongoing objective assessment of national bovine tuberculosis (bTB) policy in Ireland is important to monitor efforts towards improved bTB control. The study objective was to investigate temporal trends in the risk of herd recurrence. The study included all herds derestricted following a bTB episode ending in 1998, 2008 or 2012. The respective 'study periods' were up to the end of 2001 for 1998-derestricted herds, to the end of 2011 for 2008-derestricted herds, and to the end of 2015 for 2012-derestricted herds. A multivariable Cox proportional-hazard model was developed to examine time to next restriction. The results from the model showed a continuing significant decreasing trend in herd recurrence of bTB in Ireland from 1998 until 2015: herds derestricted in 2008 were 0.75 (95 per cent CI 0.68 to 0.82) times as likely to develop a further restriction compared with 1998 herds, and herds derestricted in 2012 were 0.85 (95 per cent CI 0.76 to 0.95) times as likely as 2008 herds. However, despite significant improvements, recurrence of bTB remains a concern, with 30.2 per cent (95 per cent CI 28.0 to 32.4 per cent) of herds derestricted in 2012 being re-restricted over the subsequent three years. Further work is needed to address the two key drivers of herd recurrence, namely residual infection and local reinfection.

An improved understanding of cattle movements, implications for disease management and surveillance (UCC component)

Humphries, R. et al.

University College Cork

This project, which is being conducted a part of a PhD, will apply a cellular automata, network based, modelling framework to cattle movements in Ireland with specific regard to disease transmission of bovine TB, and will provide a clear understanding of implications for risk-based trading.

An improved understanding of cattle movements and their implications for disease management and surveillance (UCD component)

Tratalos, J. et al.

UCD CVERA

An understanding of cattle movements is an essential component of any bovine disease control or surveillance strategy. CVERA has compiled a database of all cattle movements, as well as births, for the period 2000 – 2017. These data have been used to understand diseases such as bTB, BVD and MAP in a variety of studies. These cattle movements will be investigated further to provide an understanding of current and likely future processes and, in turn, to use this knowledge to inform disease management and surveillance.

Examining the factors which are predictive of bTB outbreak clusters in Irish cattle populations

Madden, J. et al.
UCD CVERA

Control of clustered outbreaks of bTB pose a significant challenge in bTB eradication in Ireland. The national eradication programme gathers an array of data including animal skin tests, herd level records, laboratory results and badger capture information. Utilising this rich data resource, the aim of this study was to explore historic trends in spatio-temporal variation of bTB across Ireland to identify high risk areas and determine which covariates were associated with these clusters of bTB over time. A secondary aim was to disseminate results through an R Shiny app to act as an epidemiological tool to help visualize disease spread, to assist with decision-making and potentially act as an early warning system to predict the emergence of clusters. Identifying potential risk factors for bTB clusters is a key priority for the national eradication programme. The dissemination of results and maps through an interactive app may be a valuable epidemiological tool for veterinary inspectors, both in the field and nationally.

Animal disease compensation: a comparative analysis of government approaches to compensation for the slaughter of farmed animals as a part of disease control and eradication efforts

Martin, M. et al.
DAFM

Compensation paid to owners in the event of the compulsory slaughter of farmed animals for disease control and eradication purposes represents a significant cost for many nations. Approaches to the issue vary depending upon the veterinary and epidemiological profile of the region, as well as the prevailing political and economic context. The National Farmed Animal Health Strategy (NFAHS) recommends that the national Department of Agriculture, Food and the Marine (DAFM) seeks to clarify and document the Department's expected contribution so that there is a clear understanding among all stakeholders in advance of any disease event. This study will develop a clear understanding of the rationale and operation of animal disease compensation arrangements in several different countries, to inform policy decisions.

Spatial structure of farms in Ireland

McGrath, G. et al.
UCD CVERA

This project will provide an in-depth analysis and description of the extent of farm fragmentation in Ireland, including information regarding the number of neighbours and the length of shared boundary with neighbours. The metadata will be made available as an online resource accompanying the publication, providing a reference point for future epidemiological studies and important metrics for disease modelling for use nationally and internationally as appropriate.

A visual representation of cattle movement in Ireland during 2016

McGrath, G.[1], Tratalos, J.A.[1], More, S.J.[1]

[1] UCD CVERA

Irish Veterinary Journal 71, 18 (2018)

The aim of this study was to create a clear visual representation of the live movements of cattle in the Republic of Ireland over the course of the year 2016. The animation created can be viewed online: https://youtu.be/PTCdPMnenBw. This animation was created to be a communication tool to enable stakeholders to appreciate the extent of high risk cattle movements (farm to farm, farm to market to farm) in the Republic of Ireland and to highlight the potential role that these movements may play in the spread of infectious diseases of cattle in Ireland from one farm to another.

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Can bovine TB be eradicated from the Republic of Ireland? Could this be achieved by 2030?

More, S.J.[1]

[1] UCD CVERA

Irish Veterinary Journal 72, 3 (2019)

There has been an ongoing decline in bovine tuberculosis (TB) in the Republic of Ireland, however, TB has yet to be eradicated. Further to a recent commitment by the Irish government to eradicate TB by 2030, this paper considers two questions, 'Can bovine TB be eradicated from the Republic of Ireland?' and 'Could this be achieved by 2030?', given current knowledge from research. Until very recently, Ireland has lacked key tools required for eradication. This gap has substantially been filled with the national roll-out of badger vaccination. Nonetheless, there is robust evidence, drawn from general national research, international experiences, and results of a recent modelling study, to suggest that all current strategies plus badger vaccination will not be sufficient to successfully eradicate TB from Ireland by 2030. We face a critical decision point in the programme, specifically the scope and intensity of control measures from this point forward. Adequate information is available, both from research and international experience, to indicate that these additional measures should broadly focus on adequately addressing TB risks from wildlife, implementing additional risk-based cattle controls, and enhancing industry engagement. These three areas are considered in some detail. Based on current knowledge, it will not be possible to eradicate TB by 2030 with current control strategies plus national badger vaccination. Additional measures will be needed if Ireland is to eradicate TB within a reasonable time frame. Decisions made now will have long-term implications both in terms of time-to-eradication and cumulative programme costs.

Further description of bovine tuberculosis trends in the United Kingdom and the Republic of Ireland, 2003–2015

More, S.J.[1], Houtsma, E.[1], Doyle, L.[2], McGrath, G.[1], Clegg, T.A.[1], de la Rua-Domenech, R.[3], Duignan, A.[4], Blissitt, M.J.[5], Dunlop, M.[6], Schroeder, P.G.[7], Pike, R.[8], Upton, P.[9]

[1] UCD CVERA, [2] Veterinary Epidemiology Unit, Department of Agriculture, Environment and Rural Affairs, Belfast, Northern Ireland, [3] Advice Services Team, Animal and Plant Health Agency, Bovine Tuberculosis Programme, Department of Environment, Food and Rural Affairs, London, England, [4] DAFM, [5] Veterinary and Science Team, Agriculture and Rural Economy Directorate Scottish Government, Edinburgh, Scotland, [6] Department of Agriculture, Environment and Rural Affairs, Belfast, Northern Ireland, [7] Wales Bovine TB Epidemiology Team, APHA Wales, Carmarthen, Wales, [8] TB Team, Welsh Government, Cardiff, Wales, [9] Department of Epidemiological Sciences, Animal and Plant Health Agency, Weybridge, England

Veterinary Record 183, 717 (2018)

Extending on earlier work, trends in bovine tuberculosis (bTB) from 2003 to 2015 are described for the countries of the UK and the Republic of Ireland using standardised definitions and measures. Based on measures of animal and herd incidence, there remains a stable situation of extremely low prevalence in Scotland and the Low Risk Area of England, and a higher but ongoing reduction in prevalence in the Republic of Ireland. In Northern Ireland, there has been a rising bTB trend during 2010–2015, although not to levels experienced during 2002–2004. In the High Risk Area and Edge Area of England during 2010–2015, the rising bTB trends have continued but with some recent evidence of stabilisation. In Wales, prevalence has fallen subsequent to a peak in 2008. The paper considers country-level differences in the light of key policy changes, which are presented in detail. This work is unique, and will assist policymakers when critically evaluating policy options for effective control and eradication. Ongoing updates of this analysis would be useful, providing an evidence base for country-level comparison of bTB trends into the future. The use of multivariable analytical methods should be considered, but will rely on substantial sharing of raw data across the five countries.

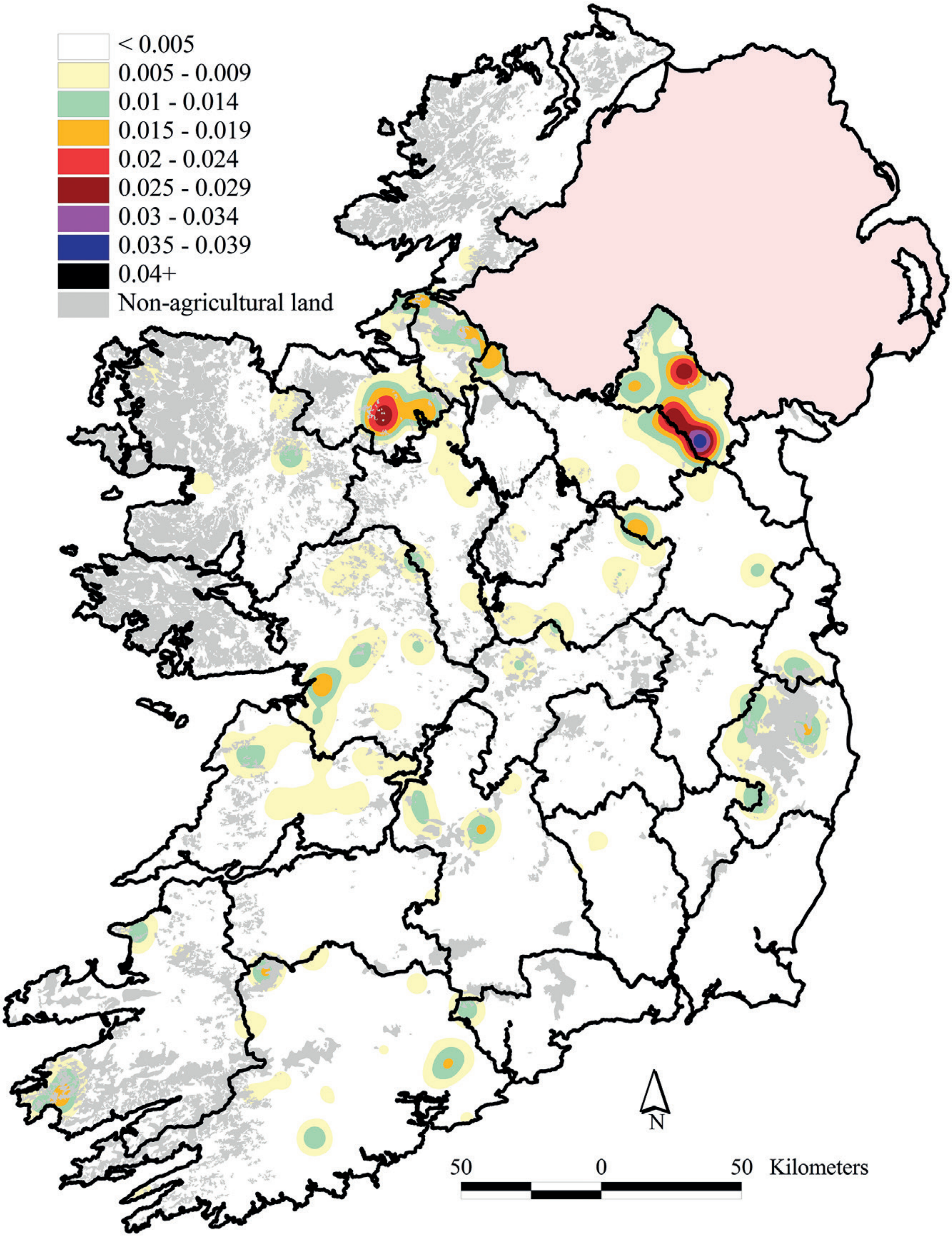
Assessment of the perceptions of stakeholders to bovine tuberculosis eradication in Ireland and the role of collaborative governance

O'Connor, J. et al.

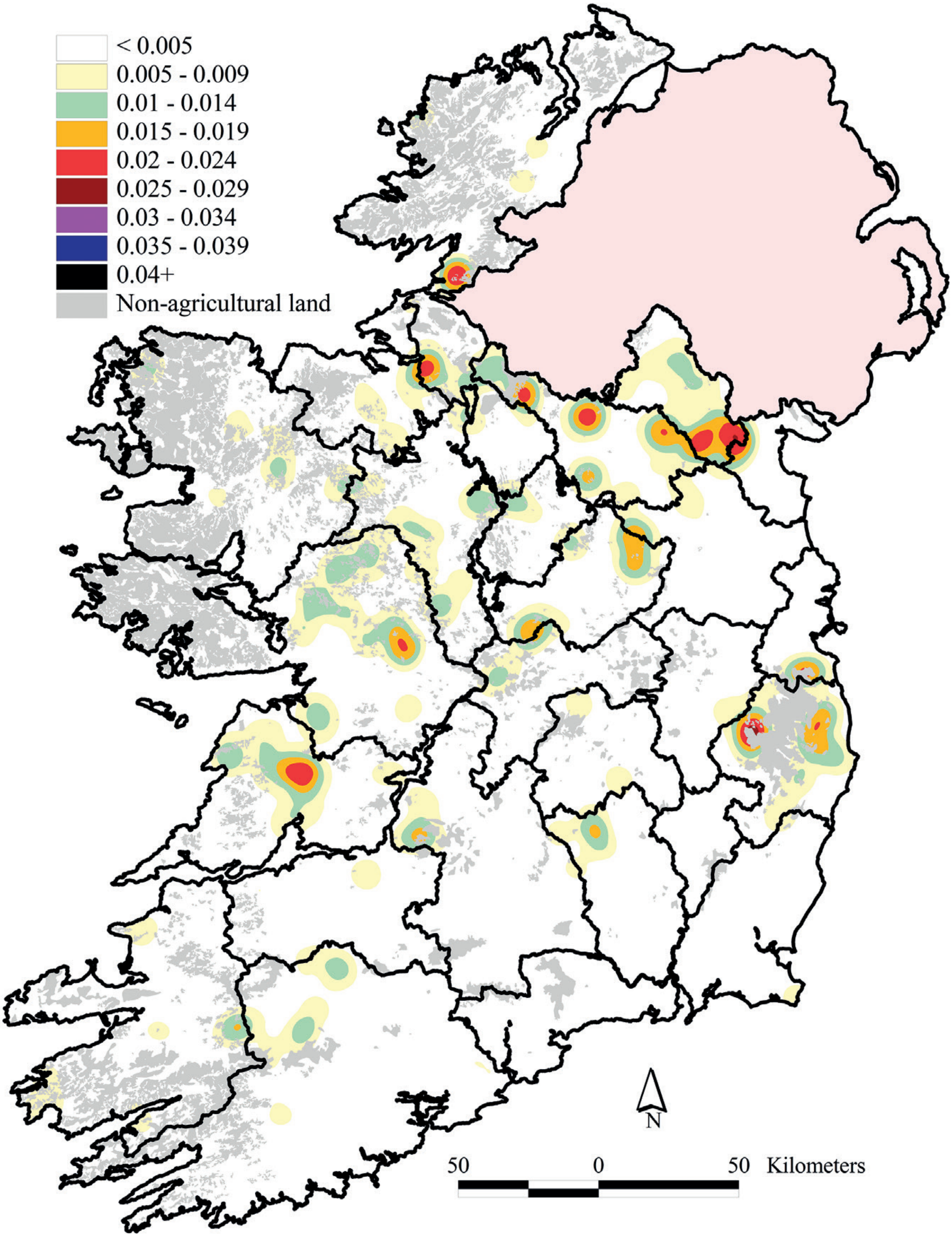
DAFM

This research has examined the attitudes and perceptions of key stakeholders of bovine tuberculosis (bTB) eradication in Ireland. The research explored the attitude of stakeholders to using a collaborative governance approach to achieve that target, given a governmental target of eradication by 2030. This research was informed by the theory of collaborative governance which holds that public administrators should directly engage non-state stakeholders in a collective decision-making process that is consensus-oriented, deliberative and that aims to make or implement public policy. A qualitative research methodology, interpretative phenomenological analysis, was used to describe, explain and understand the perspectives of study participants on bTB eradication.

Density of TB incidence

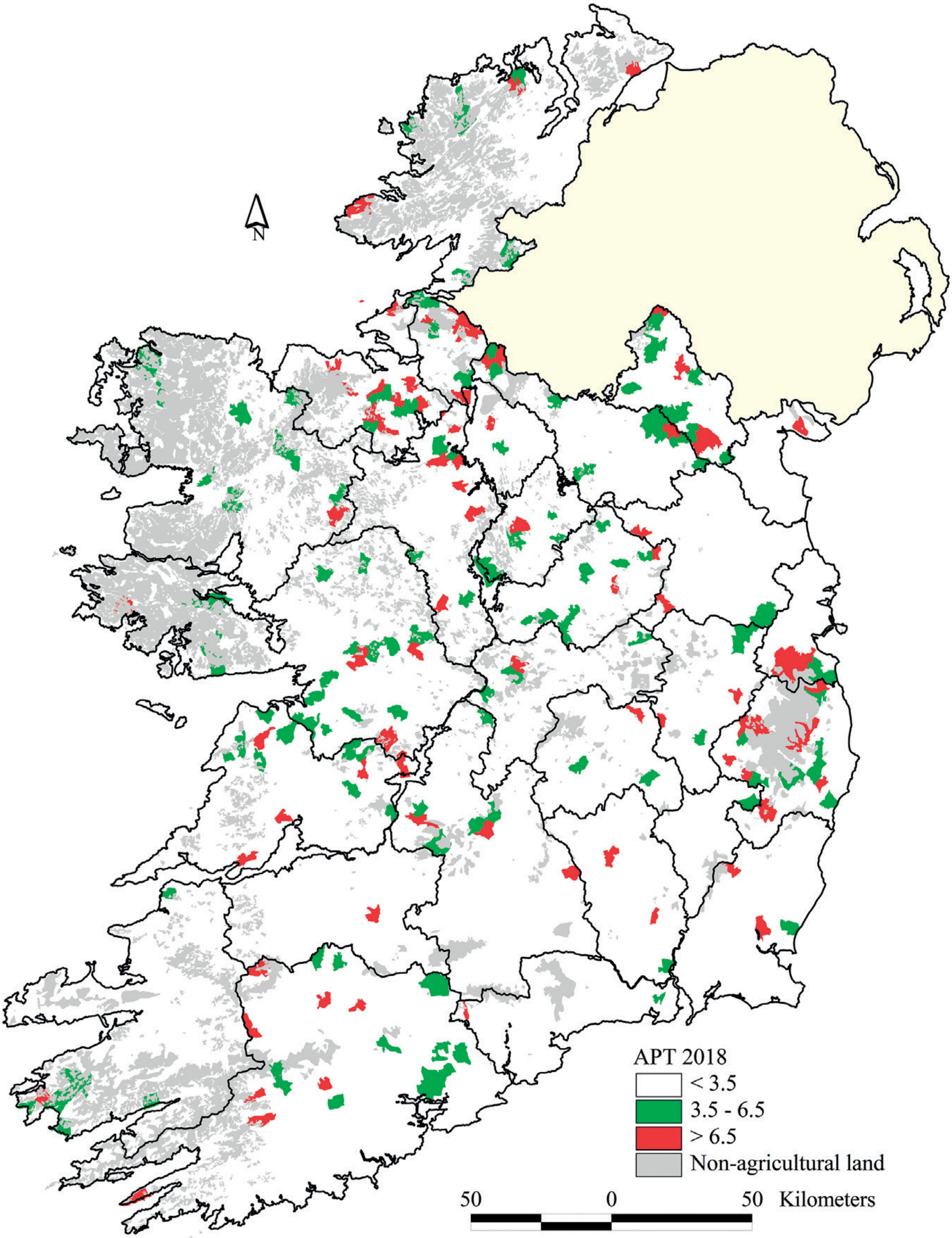


Density of TB incidence per square km during 2018 (kernel density with search radius at 10km)

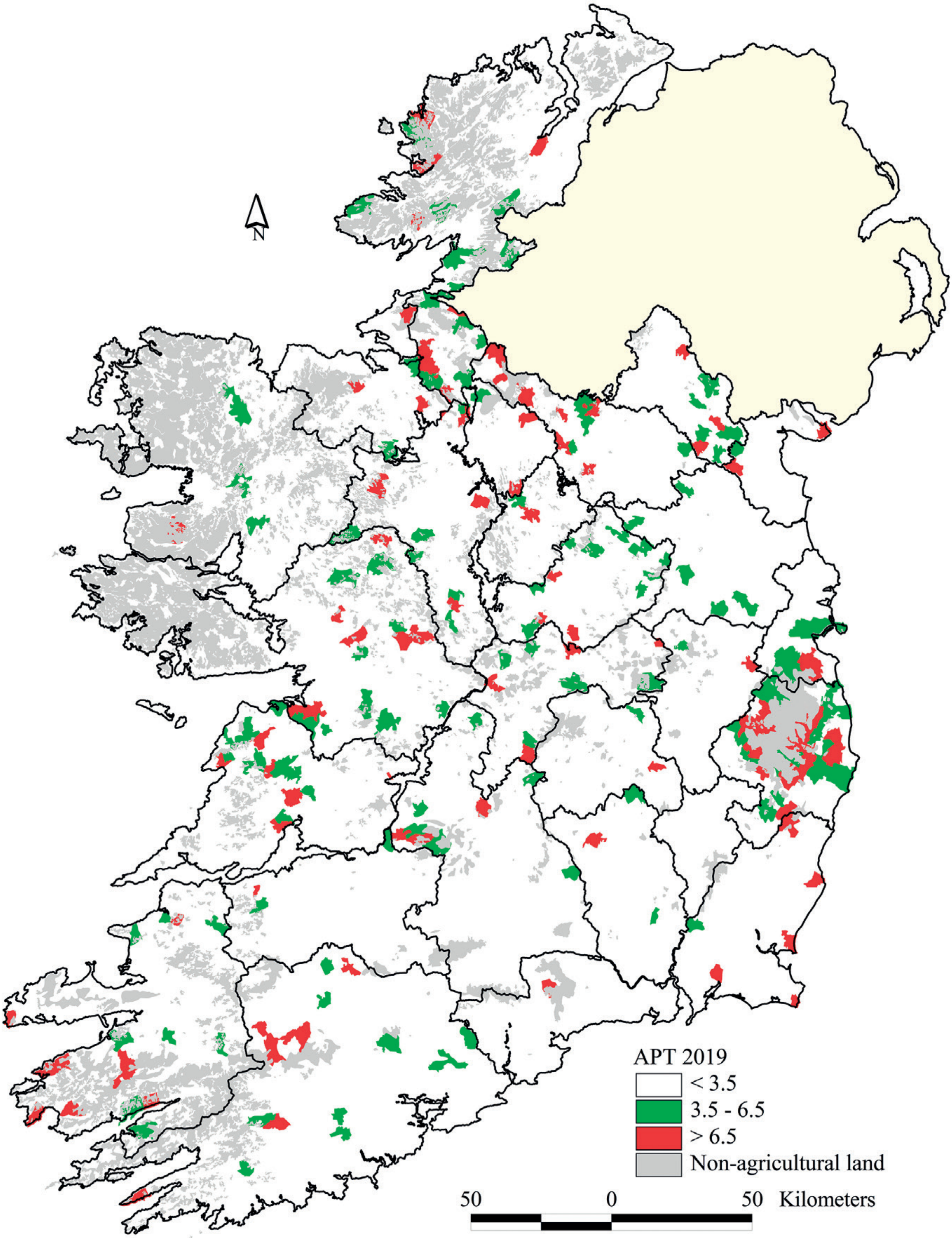


Density of TB incidence per square km during 2019 (kernel density with search radius at 10km)

APT per DED



APT (reactors per 1000 tests) per district electoral division, 2018



APT (reactors per 1000 tests) per district electoral division, 2019

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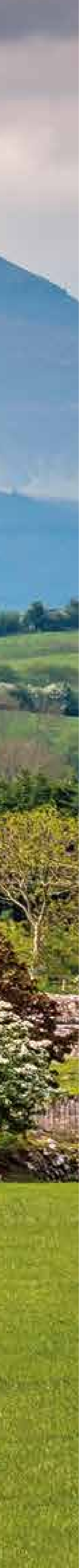

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Non-regulatory cattle health issues

Biosecure diseases

Biosecure diseases

Bovine viral diarrhoea (BVD)

Prevalence of Bovine Viral Diarrhoea Virus (BVDV), Bovine Herpes Virus 1 (BHV 1), Leptospirosis and Neosporosis, and associated risk factors in 161 Irish beef herds.

Barrett, D.[1], Parr, M.[2], Fagan, J.[3], Johnson, A.[3], Tratalos, J.[4], Lively, F.[5], Diskin, M.[6], Kenny, D.[2]

[1] DAFM, [2] Teagasc, Grange, Co. Meath, [3] DAFM Regional Veterinary Laboratory Service, [4] UCD CVERA, [5] Agri-Food and Biosciences Institute, Belfast, Co. Antrim, Northern Ireland, [6] Teagasc, Athenry, Co. Galway

BMC Veterinary Research 14, 8 (2018)

There are limited data available, in Ireland or elsewhere, to determine the extent of exposure to various endemic diseases among beef cows and factors associated with exposure to causative pathogens. The objectives of this study were to determine the herd and within herd prevalence of Bovine Viral Diarrhoea Virus (BVDV), Bovine Herpes Virus 1 (BHV-1), Leptospirosis and Neosporosis in a large scale study of commercial beef herds on the island of Ireland, and to examine herd level factors associated with exposure to these pathogens in these herds. The average number of cows tested per herd was 35.5 (median 30). Herd level seroprevalence to Bovine Herpesvirus-1(BHV-1), Bovine Viral-Diarrhoea Virus (BVDV), Leptospirosis and Neosporosis was 90%, 100%, 91% and 67%, respectively, while the mean within herd prevalence for these pathogens was 40%, 77.7%, 65.7% and 5.7%, respectively. The study confirms that the level of seroconversion for the four pathogens of interest increases with herd size. There was also evidence that exposure to one pathogen may increase the risk of exposure to another pathogen. Herd level seroprevalences were in excess of 90% for BVDV, BHV-1 and Leptosporosis. Larger herds were subject to increased exposure to disease pathogens. This study suggests that exposure to several pathogens may be associated with the further exposure to other pathogens.

Risk factors associated with the loss of negative herd status (NHS) for BVD in 548 Irish cattle herds

Barrett, D. et al.
DAFM

Considerable progress has been made over the course of the BVD eradication programme in Ireland since it commenced in 2012, with over 72,000 herds achieving BVD negative herd status (NHS) in 2017. However, 546 herds which had been assigned NHS status at the start of 2017, lost that status during 2017 due to the birth of one or more PI calves. The loss of NHS in these herds is a cause of concern. The objective of the study was to determine the risk factors associated with the loss of BVD negative herd status in 546 herds in 2017.

Herd and animal-level clustering of BVDV - assessment of influence of neighbours and transboundary impacts

Casey, M. et al.
UCD CVERA

The national BVD eradication programme has made significant progress since 2013. A previous study on risk factors for re-infection of previously BVD-free herds in Ireland identified the density of cattle persistently infected with BVD virus within 10 km as significant. A parallel eradication programme, based on a common tissue-tag testing approach, is also being implemented in Northern Ireland. While the issue of retention of persistently infected animals (PIs) has essentially been resolved in Ireland, it remains a significant challenge in NI. As a consequence, there is a marked disparity between the numbers of PIs alive in each jurisdiction (approximately 16:1 NI:ROI at the start of 2019, despite a fourfold higher cattle population in ROI). This raises the possibility that herds in ROI, but close to the border with NI, will have a higher risk of a BVD 'breakdown' and therefore require a particular focus on biosecurity to address this. More generally, assessing the spatial distribution of herds in which PI calves are born can provide further insights into the density effect described above and contribute to outbreak investigations and identification of transmission pathways. While the particular focus of the study is on BVD, the outcomes will also have relevance to the spread of other disease and be informative in appropriate measures for their control. This study is particularly timely in the context of Brexit.

Exploring perceptions of, and future challenges facing, animal health in Ireland

Meunier, N. et al.
Animal Health Ireland

Animal Health Ireland (AHI) has conducted a survey exploring the changes in the awareness and perception of a number of animal health issues since AHI was founded in 2009. The project also seeks to identify animal health and welfare challenges to be addressed over the next decade.

Investigation of the potential for sera from cattle persistently infected with bovine viral diarrhoea virus to generate false-negative antibody ELISA results in pooled serum from seropositive and seronegative cattle

Graham, D.A.[1], King, D.[1], Clegg, T.A.[2], O'Neill, R.G.[3]

[1] Animal Health Ireland, [2] UCD CVERA, [3] DAFM Veterinary Laboratory Service

Journal of Veterinary Diagnostic Investigation 31, 284-288 (2019)

We investigated the potential for viremic sera from cattle persistently infected with bovine viral diarrhea virus to create false-negative antibody results when testing pools of 10 sera by indirect or blocking ELISAs. Seronegative viremic sera (*n* = 23) were each added to a series of artificially constructed pools containing various percentages (0–90%) of antibody-positive sera, and the resulting pools were assayed for antibody. In all 23 cases, a negative antibody result was obtained in the pool containing no seropositive sera. In contrast, all pools containing ≥10% seropositive serum, representing a single seropositive animal in a pool of 10 samples, returned a positive result in both antibody ELISAs. We concluded that the likelihood of a false-negative antibody result occurring as a result of the presence of serum from a viremic animal was low, and therefore did not preclude the use of pooled sera for serosurveillance.

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Potential infection-control benefit of measures to mitigate the risk posed by Trojan dams in the Irish BVD eradication programme

Reardon, F.[1]**, Graham, D.**[2]**, Clegg, T.A.**[1]**, Tratalos, J.A.**[1]**, O'Sullivan, P.**[3]**, More, S.J.**[1]

[1] UCD CVERA, [2] Animal Health Ireland, [3] Irish Cattle Breeding Federation

Preventive Veterinary Medicine 157, 78-85 (2018)

In the epidemiology of Bovine Viral Diarrhoea (BVD), Trojan dams (animals that are not persistently infected (PI) with BVD (BVDv) virus but carrying PI foetuses) are a vehicle through which infection can be transmitted. We investigated the degree to which restricting movement of cattle from BVDv infected herds would prevent Trojan births in other herds (effectiveness) and the extent to which this would reduce other, non-Trojan, movements (proportionality). We focussed on Irish herds with BVD + animal(s) present during 2014 and/or 2015. The effect of restricting movements of female animals over 12 months of age from these herds was compared with data collected on Trojan dams that calved in 2015. Four different potential restriction lengths were considered, varying from the period when a BVD + animal was present in the herd, to extending this to 12 months after removal of the last BVD + animal. In terms of effectiveness, none of the four restriction measures evaluated was effective at preventing the movement of all Trojan dams. Between 18.3% and 37.3% of Trojan births in 2015 would have been prevented under the proposed measures, and all Trojan births would have been prevented in between 14.4% and 32.5% of herds with BVD + births. In terms of proportionality, between 4.4% and 15.4% of all females > 12 months of age that moved between herds during 2015 would have been prevented from moving, and between 3.5% and 10.1% of Irish herds with at least one such movement would have been affected. These results show how measures to control the movement of Trojan dams should be targeted in a way that fits the Irish context and reduces the spread of BVDv, without unduly impacting other trade.

Reprinted from Preventive Veterinary Medicine*, 157, Reardon et al, Potential infection-control benefit of measures to mitigate the risk posed by Trojan dams in the Irish BVD eradication programme, 78-85, Copyright 2018, with permission from Elsevier.*

Quantifying the role of Trojan dams in the between-herd spread of bovine viral diarrhoea virus (BVDv) in Ireland

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Preventive Veterinary Medicine 152, 65-73 (2018)

A compulsory national programme to eradicate bovine viral diarrhoea virus (BVDv) began in Ireland on 1 January, 2013. The objective of the current study was to quantify the role of Trojan dams (animal(s) not persistently infected (PI) with BVDv but carrying PI foetus(es) and introduced to the herd while pregnant with the PI foetus(es)) in the farm-to-farm spread of BVDv in Ireland, and to identify herd-level risk factors for producing or introducing a Trojan dam. The study population included all BVD+ calves born in Ireland between 1 January, 2013 and 31 December, 2015, along with their dams. BVD+ calves included all calves on the national programme database with an initial positive or inconclusive virus test, without a confirmatory re-test (status BVDPOS) and those with an initial positive or inconclusive test and a positive confirmatory test (status BVDPI). The Trojan status of dams was determined after considering their history of movement and of potential BVDV exposure, relative to a defined window of susceptibility (WOS; days 30–120 of gestation). During 2013–15, there were 29,422 BVD+ birth events to dams that were not themselves BVD+, including 2526 (8.6%) most-likely attributable to Trojan dams. The percentage of these birth events attributable to Trojan dams was significantly different ($P < 0.001$) between years, being 7.1% in 2013, 9.2% in 2014 and 10.6% in 2015. During 2013, in 9.9% of herds with one or more BVD+ birth to non-BVD+ dams, at least one of these births was attributed to a Trojan dam. In 2014 and 2015, the percentages were 11.8% and 13.3%, respectively. In 2013, in 7.8% of herds with one or more BVD+ birth to non-BVD+ dams, all of these births were attributable to Trojan dams. In 2014 and 2015, the percentages were 9.2% and 10.7%, respectively. A logistic GEE regression identified dam parity, herd size and an interaction between herd type and season as significant predictors for the birth of a BVD+ calf to a Trojan dam. Significant predictors for the sale of a Trojan dam from BVD+ herds included those selling more than one pregnant female and those with more than 2 BVD+ animals in the herd. Introduction of pregnant adult females is a potential source of BVD+ births in BVD-free herds and may add to the burden of infection in non-BVD-free herds. Addressing this route of transmission will be critical for herds that are now free of infection and wish to continue to purchase animals without introducing it.

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Eradicating BVD, reviewing Irish programme data and model predictions to support prospective decision making

Thulke, H.-H.[1], Lange, M.[1], Tratalos, J.A.[2], Clegg, T.A.[2], McGrath, G.[2], O'Grady, L.[3], O'Sullivan, P.[4], Doherty, M.L.[3], Graham, D.A.[5], More, S.J.[2]

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Preventive Veterinary Medicine 150, 151-161 (2018)

Bovine Viral Diarrhoea is an infectious production disease of major importance in many cattle sectors of the world. The infection is predominantly transmitted by animal contact. Postnatal infections are transient, leading to immunologically protected cattle. However, for a certain window of pregnancy, in utero infection of the foetus results in persistently infected (PI) calves being the major risk of BVD spread, but also an efficient target for controlling the infection. There are two acknowledged strategies to identify PI animals for removal: tissue tag testing (direct; also known as the Swiss model) and serological screening (indirect by interpreting the serological status of the herd; the Scandinavian model). Both strategies are effective in reducing PI prevalence and herd incidence. During the first four years of the Irish national BVD eradication programme (2013–16), it has been mandatory for all newborn calves to be tested using tissue tag testing. During this period, PI incidence has substantially declined. In recent times, there has been interest among stakeholders in a change to an indirect testing strategy, with potential benefit to the overall programme, particularly with respect to cost to farmers. Advice was sought on the usefulness of implementing the necessary changes. Here we review available data from the national eradication programme and strategy performance predictions from an expert system model to quantify expected benefits of the strategy change from strategic, budgetary and implementation points of view. Key findings from our work include (i) drawbacks associated with changes to programme implementation, in particular the loss of epidemiological information to allow real-time monitoring of eradication progress or to reliably predict time to eradication, (ii) the fact that only 25% of the herds in the Irish cattle sector (14% beef, 78% dairy herds) would benefit financially from a change to serosurveillance, with half of these participants benefiting by less than EUR 75 per annum at herd level or an average of EUR 1.22 per cow, and (iii) opportunities to enhance the effectiveness of the current programme, particularly in terms of time to eradication, through enforced compliance with PI removal as currently outlined in programme recommendations. The assembled information provides scientific arguments, contributing to an informed debate of the pros and cons of a change in eradication strategy in Ireland.

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Post-eradication options for BVD surveillance in the Irish cattle population

Thulke, H.-H. et al.

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Ireland is rapidly moving towards BVD eradication. The new Animal Health Law legislates minimum standards for BVD free status for regions and Member States in order to allow intra-union trade. Effective and economically feasible BVD surveillance post-eradication requires the testing of possible options in the context of new introductions to a population just freed from the infection. The scenario addresses a future situation and requires assessment of the performance of different surveillance strategies under conditions not yet covered by observational data. A systematic approach is required, combining available epidemiological knowledge with the dynamics of reintroduced BVD into a naïve cattle population reflecting Irish production system. The recent experience with the planning of the Irish eradication programme using an epidemiological expert system has led to the development of appropriate software for the strategic and economic assessment of post-eradication BVD surveillance strategies. The project will implement this software to analyse the performance of surveillance options. The results will be presented to stakeholders to ensure that programme decisions are scientifically robust whist also adhering to the requirements of European Animal Health laws.

Sampling methodology to maximise the efficient use of national abattoir surveillance: using archived sera to substantiate freedom from bluetongue virus infection in Ireland

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Frontiers in Veterinary Science 5, 261 (2018)

In recent years, there has been increasing recognition of the value of multiple data sources available to fulfill surveillance objectives, and the use of these has been applied to address many questions relating to animal health surveillance. In Ireland, we face a slightly different problem, namely, best use of an existing surveillance resource (serological samples collected over many years from cull cows at slaughter), which has been used to substantiate freedom from Brucella abortus following its successful eradication in 2009. In this study, we evaluate a sampling methodology to use this resource to substantiate freedom from bluetongue virus (BTV) infection. An examination of the degree to which cull cows were resident in the same herd throughout the midge biting season showed that, of 50,640 samples collected between 17 October and 23 December 2016, 80.2% were from animals resident in the same herd between 01 April 2016 and 2 months prior to their slaughter date, 74.1% for 1 month prior, 70.1% for 2 weeks prior, 66.4% for 1 week prior, and 56.4% up to 1 day prior to slaughter. An examination was made of the degree to which individual samples within the same 88-well frozen storage block came from geographically clustered herds, whether from a concentration of animals from the same herd in a single block, or from clustering around the slaughterhouse where the samples were taken. On the basis of these analyses, a sampling strategy was derived aimed at minimizing the number of storage blocks which needed to be thawed, whilst ensuring a large enough and representative sample, geographically stratified according to the bovine population of 51 squares, each 45 × 45 km, covering the entirety of Ireland. None of the 503 samples tested were positive for BTV, providing reassurance of national BTV freedom. More broadly, the study demonstrates the use of abattoir-based serological samples collected for one large scale surveillance programme in surveillance for other bovine infections.

Decision support beyond total savings - eligibility and potential savings for individual participants from changes in the national surveillance strategy for bovine viral diarrhoea (BVD) in Ireland

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Preventive Veterinary Medicine 155, 38-44 (2018)

Surveillance and management of livestock diseases is often evaluated with reference to expected sector-wide costs. In contrast, we calculate losses or savings for individual herd owners of a change in monitoring strategy during a national cattle disease eradication programme: bovine viral diarrhoea (BVD) in Ireland. The alternative strategy differs in how the disease is identified; by its sample- rather than census-based approach; and by its greater cost per test. We examined the costs faced by each breeding herd if testing were conducted using serology on a sample of young stock, in contrast to the current method of tissue-tag testing of all newborn calves. Following best knowledge of the likely costs, the following input values were used: i) €2.50 per test for tissue-tag testing and €7.66 for serology, ii) serology conducted on a sample of 10 young stock per management group from either the 6–12 month or 9–18 month cohorts; iii) 3 scenarios for the number of management groups: one per herd (M∞), one per 100 cows (M100) and one per 50 cows (M50). We found that many herds would often not be able to supply a suitable sample of young stock for serology or would face higher testing costs than when using tissue tag testing. The largest number (25%) of herds would benefit from participating in the change if sampling were done in October. These could annually save between €2.1 million under M∞ and €0.8 million under M50 (€108 - €49 per herd). However, analysing herd-level data we found that 90% of all Irish breeding herds would save less than €1.42 per cow or €99 in total per annum under M∞, and €0.59 per cow or €36 in total under M50. In a sensitivity analysis, we allowed serology costs to vary between €2 and €10 per animal. Herds at the 10th percentile of most savings made from switching would save at most €155 (M∞ at €2 per serology test) but would not save anything under M50 at costs ≥ €10. We conclude that, under these assumptions, the expected reduction in testing costs for the majority of beneficiaries would barely outweigh the practical implications of the strategy switch or the risks to the eradication programme associated with sample-based surveillance. This study does not assess the cost-effectiveness of alternatives post-eradication.

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STOC Free: an innovative framework to compare probability of freedom from infection in heterogeneous control programmes

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Frontiers in Veterinary Science 6, 133 (2019)

The existence, stage of eradication and design of control programmes (CPs) for diseases that are not regulated by the EU differ between Member States. When freedom from infection is reached or being pursued, safe trade is essential to protect or reach that status. The aim of STOC free, a collaborative project between six countries, is to develop and validate a framework that enables a transparent and standardized comparison of confidence of freedom for CPs across herds, regions or countries. The framework consists of a model combined with a tool to facilitate the collection of the necessary parameters. All relevant actions taken in a CP are included in a Bayesian network model, which allows prior distributions for most parameters. In addition, frequency of occurrence and risk estimates for factors that influence either the probability of introduction or temporary misclassification leading to delayed detection of the infection are included in the model. Bovine viral diarrhoea virus (BVDV) is used as an example disease. Many countries have CPs in place for BVDV and although elements of the CPs are similar, biosecurity measures and testing protocols, including types of tests and testing frequency, as well as target groups, differ widely. Although the initially developed framework is based on BVDV, the aim is to make it sufficiently generic to be adaptable to CPs for other diseases and possibly other species. Thus, STOC free will result in a single general framework, adaptable to multiple disease CPs, which aims to enhance the safety of trade.

A description and qualitative comparison of the elements of heterogeneous Bovine Viral Diarrhea control programs that influence confidence of freedom

van Roon, A.M. et al.

Department of Farm Animal Health, Faculty of Veterinary Medicine, Utrecht University, Utrecht, Netherlands

Countries worldwide have implemented control or eradication programmes to regulate endemic infections in cattle. The ‘free’ status of cattle from these programmes are difficult to compare; therefore, trade poses an ongoing risk for (re-)introduction of infection. This study is part of the larger STOC free project, representing the first step towards the development of a practical field-based tool for comparison of confidence of freedom achieved by control programmes across territories. We describe and compare elements of these programmes that contribute to confidence of freedom. The results highlight considerable heterogeneity between programmes, and the need to combine many elements about control programmes and their context into an output-based framework.

STOC free: Comparison of the confidence in freedom from infection based on different control programmes between EU member states

van Roon, A.M. et al.
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Several European countries have implemented programmes to control or eradicate non-regulated diseases of cattle. These programmes create difficulties with intra-community trade as free trade of livestock between member states has the potential to allow the movement of infectious agents to regions where freedom from infection has been achieved. There is a need for a simple and practical field-based application to enable the outputs from control programmes (specifically the confidence of freedom from infection) to be compared in a standardised and quantitative way. This project uses bovine viral diarrhoea as an example disease. This project will development of a framework, including a model (STOC free MODEL) and a data collection tool (STOC free DATA), to provide an objective and uniform approach to assess the probability of freedom from infection and its associated uncertainty, after accounting for the heterogeneity in context and design of the control programme.

Infectious bovine rhinotracheitis (IBR)

Evaluating an IBR eradication programme

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IBR is a highly contagious bovine disease caused by the bovine herpes virus type 1 (BoHV-1). Infections with BoHV-1 are often associated with various clinical manifestations, such as fever, reduced, growth/milk release and an increased risk of death and abortion. It is estimated that in Ireland more than 80% of all herds have BoHV-1 infections, with the potential for substantial economic losses. The feasibility of a national BoHV-1 eradication campaign is currently under consideration in Ireland. In order to support discussion and to quantitatively assess the efficacy of various control strategies, a national BoHV-1 simulation model will be developed within the framework of this project.

Reviewing age-structured epidemiological models of cattle diseases tailored to support management decisions: guidance for the future

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Preventive Veterinary Medicine (in press)

Mechanistic simulation models are being increasingly used as tools to assist with animal health decision-making in the cattle sector. We reviewed scientific literature for studies reporting age-structured cattle management models in application to infectious diseases. Our emphasis was on papers dedicated to support decision making in the field. In this systematic review we considered 1290 manuscripts and identified 76 eligible studies. These are based on 52 individual models from 10 countries addressing 9 different pathogens. We provide an overview of these models and present in detail their theoretical foundations, design paradigms and incorporated processes. We propose a structure of the characteristics of cattle disease models using three main features: [1] biological processes, [2] farming-related processes and [3] pathogen-related processes. It would be of benefit if future cattle disease models were to follow this structure to facilitate science communication and to allow increased model transparency.

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Johne's disease

NexusMAP - developing an expert system model to support national decision-making

Biemans, F. et al.

UCD CVERA

An existing spatio-temporal transmission model for Johne's disease is available, accounting for population and infection dynamics, and simulating transmission of infection within and between dairy farms in Brittany, France. The model was developed by colleagues at BIOEPAR, Nantes, France. In a collaboration between BIOEPAR, CVERA and Animal Health Ireland, French model is currently being adapted to Irish conditions, including the incorporation of Irish cattle movement data. Several intervention strategies are being investigated with the aim to support decision-making for the national voluntary Johne's control programme.

Low accuracy of Bayesian latent class analysis for estimation of herd-level true prevalence under certain disease characteristics - An analysis using simulated data

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Preventive Veterinary Medicine 162, 117-125 (2019)

Estimation of the true prevalence of infected individuals involves the application of a diagnostic test to a population and adjusting according to test performance, sensitivity and specificity. Bayesian latent class analysis for the estimation of herd and animal-level true prevalence, has become increasingly used in veterinary epidemiology and is particularly useful in incorporating uncertainty and variability into analyses in a flexible framework. However, the approach has not yet been evaluated using simulated data where the true prevalence is known. Furthermore, using this approach, the within-herd true prevalence is often assumed to follow a beta distribution, the parameters of which may be modelled using hyperpriors to incorporate both uncertainty and variability associated with this parameter. Recently however, the authors of the current study highlighted a potential issue with this approach, in particular, with fitting the distributions and a tendency for the resulting distribution to invert and become clustered at zero. Therefore, the objective of the present study was to evaluate commonly specified models using simulated datasets where the herd-level true prevalence was known. The specific purpose was to compare findings from models using hyperpriors to those using a simple beta distribution to model within-herd prevalence. A second objective was to investigate sources of error by varying characteristics of the simulated dataset. Mycobacterium avium subspecies paratuberculosis infection was used as an example for the baseline dataset. Data were simulated for 1000 herds across a range of herd-level true prevalence scenarios, and models were fitted using priors from recently published studies. The results demonstrated poor performance of these latent class models for diseases characterised by poor diagnostic test sensitivity and low within-herd true prevalence. All variations of the model appeared to be sensitive to the prior and tended to overestimate herd-level true prevalence. Estimates were substantially improved in different infection scenarios by increasing test sensitivity and within-herd true prevalence. The results of this study raise questions about the accuracy of published estimates for the herd-level true prevalence of paratuberculosis based on serological testing, using latent class analysis. This study highlights the importance of conducting more rigorous sensitivity analyses than have been carried out in previous analyses published to date.

A review of paratuberculosis in dairy herds – Part 1: Epidemiology

McAloon, C.G.[1], Roche, S.[2], Ritter, C.[3], Barkema, H.W.[3], Whyte, P.[1], More, S.J.[4], O'Grady, L.[1], Green, M.J.[5], Doherty, M.L.[1]

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The Veterinary Journal 246, 59-65 (2019)

Bovine paratuberculosis is a chronic infectious disease of cattle caused by *Mycobacterium avium* subspecies *paratuberculosis* (MAP). This is the first in a two-part review of the epidemiology and control of paratuberculosis in

dairy herds. Paratuberculosis was originally described in 1895 and is now considered endemic among farmed cattle worldwide. MAP has been isolated from a wide range of non-ruminant wildlife as well as humans and non-human primates. In dairy herds, MAP is assumed to be introduced predominantly through the purchase of infected stock with additional factors modulating the risk of persistence or fade-out once an infected animal is introduced. Faecal shedding may vary widely between individuals and recent modelling work has shed some light on the role of super-shedding animals in the transmission of MAP within herds. Recent experimental work has revisited many of the assumptions around age susceptibility, faecal shedding in calves and calf-to-calf transmission. Further efforts to elucidate the relative contributions of different transmission routes to the dissemination of infection in endemic herds will aid in the prioritisation of efforts for control on farm.

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A review of paratuberculosis in dairy herds – Part 2: On-farm control

McAloon, C.G.[1], Roche, S.[2], Ritter, C.[3], Barkema, H.W.[3], Whyte, P.[1], More, S.J.[4], O'Grady, L.[1], Green, M.J.[5], Doherty, M.L.[1]

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The Veterinary Journal 246, 54-58 (2019)

Bovine paratuberculosis is a chronic infectious disease of cattle, caused by *Mycobacterium avium* subspecies *paratuberculosis* (MAP). This is the second in a two-part review of the epidemiology and control of paratuberculosis in dairy herds. Several negative production effects associated with MAP infection have been described, but perhaps the most significant concern in relation to the importance of paratuberculosis as a disease of dairy cattle is the potential link with Crohn's disease in humans. Milk is considered a potential transmission route to humans and it is recognised that pasteurisation does not necessarily eliminate the bacterium. Therefore, control must also include reduction of the levels of MAP in bulk milk supplied from dairy farms. There is little field evidence in support of specific control measures, although several studies seem to show a decreased prevalence associated with the implementation of a combined management and test-and-cull programme. Improvements in vaccination efficacy and reduced tuberculosis (TB) test interference may increase uptake of vaccination as a control option. Farmer adoption of best practice recommendations at farm level for the control of endemic diseases can be challenging. Improved understanding of farmer behaviour and decision making will help in developing improved communication strategies which may be more efficacious in affecting behavioural change on farm.

Reprinted from The Veterinary Journal*, 246, McAloon et al, A review of paratuberculosis in dairy herds – Part 2: On-farm control, 54-58, Copyright 2019, with permission from Elsevier.*

Modeling of alternative testing strategies to demonstrate freedom from *Mycobacterium avium* ssp. *paratuberculosis* infection in test-negative dairy herds in the Republic of Ireland

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Journal of Dairy Science 102, 2427-2442 (2019)

In light of the various adverse effects of Johne's disease on animal productivity and the debate on the role of its causative organism, *Mycobacterium avium* ssp. *paratuberculosis*, in the etiology of Crohn's disease, major dairy-producing countries around the world have implemented national control programs aimed at reducing the prevalence of this infection in cattle. A pilot control program was initiated in Ireland in 2013, with a key objective to provide farmers with test-negative dairy herds with tools and knowledge to increase their confidence of freedom over time. The aim of this study was to estimate the confidence of freedom obtained in test-negative Irish dairy herds over time with various sampling scenarios and to evaluate the cost-effectiveness of alternative scenarios for achieving an acceptable level of confidence of freedom in herds with no evidence of infection. A stochastic model was developed to simulate repeated annual testing of individual animals using ELISA and confirmatory assays over a period of 20 yr. Two scenarios modeled the current herd-screening options, whereas 14 alternative scenarios explored the effect of varying parameters from the current testing strategies, such as the frequency of testing, the eligibility criteria for selecting animals, the type of assay, the probability of introduction, and the assay sensitivity. Results showed that the current testing strategy with milk twice a year or serum once a year in all animals over 2 yr old provided the highest annual herd sensitivity, with a median value of 55%. Although the median confidence of freedom increased over time for all scenarios, the time required to reach 90 and 95% confidence of freedom was highly variable between scenarios. Under the testing scenario where serum tests were used once a year, the confidence of freedom reached 90% after 4 yr and 95% after 7 yr of testing. Some of the alternative scenarios achieved an acceptable level of confidence of freedom in a reasonable timeframe and at lesser cost than the current testing strategies. The results of this work are used to provide recommendations for the next phases of the program.

Evaluation of national surveillance methods for detection of Irish dairy herds infected with *Mycobacterium avium* subspecies *paratuberculosis*

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Journal of Dairy Science 102, 2525-2538 (2019)

The aim of this study was to evaluate the utility and cost-effectiveness of a range of national surveillance methods for paratuberculosis in Irish dairy herds. We simulated alternative surveillance strategies applied to dairy cattle herds for the detection of *Mycobacterium avium* ssp. *paratuberculosis* (MAP)-infected herds (case-detection) or for estimation of confidence of herd freedom from infection (assurance testing). Strategies simulated included whole-herd milk or serum serology, serology on cull cows at slaughter, bulk milk tank serology, environmental testing, and pooled fecal testing. None of the strategies evaluated were ideal for widespread national case-detection surveillance. Herd testing with milk or serum ELISA or pooled fecal testing were the most effective methods currently available for detection of MAP-infected herds, with median herd sensitivity >60% and 100% herd specificity, although they are relatively expensive for wide-

spread use. Environmental sampling shows promise as an alternative, with median herd sensitivity of 69%, but is also expensive unless samples can be pooled and requires further validation under Irish conditions. Bulk tank milk testing is the lowest cost option and may be useful for detecting high-prevalence herds but had median herd sensitivity <10% and positive predictive value of 85%. Cull cow sampling strategies were also lower cost but had median herd sensitivity <40% and herd positive predictive values of <50%, resulting in an increased number of test-positive herds, each of which requires follow-up herd testing to clarify status. Possible false-positive herd testing results associated with prior tuberculosis testing also presented logistical issues for both cull cow and bulk milk testing. Whole-herd milk or serum ELISA testing are currently the preferred testing strategies to estimate confidence of herd freedom from MAP in dairy herds due to the good technical performance and moderate cost of these strategies for individual herd testing. Cull cow serology and bulk tank milk sampling provide only minimal assurance value, with confidence of herd freedom increasing only minimally above the prior estimate. Different testing strategies should be considered when deciding on cost-effective approaches for case-detection compared with those used for building confidence of herd freedom (assurance testing) as part of a national program.

Johne's disease in Irish dairy herds: considerations for an effective national control programme

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Johne's disease is a significant disease of cattle with possible public health implications. This has led to the development of national control programmes throughout the world. The unique epidemiology of Johne's disease means that traditional regulatory control programmes tend to fail. This paper presents key issues that influence control of Johne's disease and evaluates the likely effectiveness of different approaches to achieve the industry-agreed objectives of the Irish Johne's Control Program (IJCP).

Surveillance Welfare and Biosecurity of farmed animals in Ireland (SWAB)

McAloon, C. et al.
UCD School of Veterinary Medicine

Emerging and re-emerging diseases are a major and growing threat to the agricultural industry, with severe economic impacts. As a result, early detection is extremely important in order to minimise damage. However, currently used surveillance systems depend on detection of specific pathogens or screening at-risk populations of animals and are therefore not necessarily suitable for the detection of novel or unexpected diseases. This project aims to use syndromic surveillance techniques for the early detection of emerging diseases in Irish dairy cattle. This will involve using routinely collected data (milk yield, reproductive data, mortality, etc.) and establish acceptable levels of variation. Breaches of these acceptable levels shall be used to set "alarms" for potential incidences of disease. Schmallenberg surveillance data will then be used to assess the value of utilising this technique for early detection of disease. This will require routinely collected data from existing databases, which includes milk production data, fertility data (specifically calving dates and insemination dates), and mortality data. Variables will be modelled in time and space requiring location data for each herd. These methods will then be used to investigate farm level security measures.

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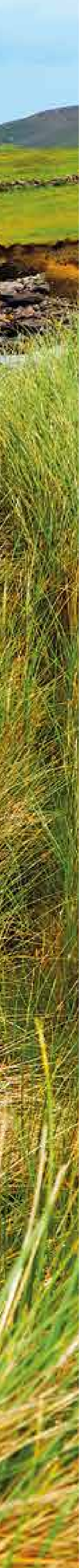

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Other animal health and welfare issues

Animal welfare

Challenges and solutions to supporting farm animal welfare in Ireland: responding to the human element

Devitt, C.[1], Hanlon, A.[2], More, S.J.[3], Kelly, P.C.[4], Blake, M.[4]

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Over recent decades, changes in agriculture have pushed animal welfare as a topic of concern into mainstream public, policy and political conversations. Despite the relationship between farmers and farm animals being important for farm animal welfare standards, there is limited understanding of how the nature of this relationship influences welfare outcomes. Understanding the complexities of this relationship and the wider context in which these complexities are situated is central to forming and implementing interventions that can be effective in improving farm animal welfare on individual farms. Overall, this report aims to:

1) Increase national and international awareness of the centrality of the relationship between human welfare and farm animal welfare, and of the challenges experienced by veterinary professionals who encounter complex farm animal welfare situations. This report will be of significant interest to a transdisciplinary audience comprising policy makers and animal welfare legislators; practitioners involved in farm veterinary care and inspection, and in human health; farm, rural and animal welfare advocacy groups; and academics involved in the social, health and veterinary sciences. The report will also be of benefit to those advocating for the One Welfare concept;

2) Introduce the One Welfare concept with the aim of providing practical guidance to assist stakeholders, policy makers and legislators in the formation and delivery of farm animal welfare support interventions that are farmer and animal-centred– including approaches aimed at building on-farm capacity and compliance with animal welfare legislation. It is hoped that this report will contribute to further conversations on the practical application of the One Welfare concept; and

3) Ultimately, this report hopes to assist legislators, policy makers, and practitioners in reducing the number of farm animal incidents and improving farm animal welfare standards.

Available at: http://hdl.handle.net/10197/10470

An evaluation of private standards in animal health and welfare and associated quality assurance programmes

Marchewka, J. et al.

Institute of Genetics and Animal Breeding of the Polish Academy of Sciences, Magdalena, Poland

In recent years, 'private standards' in animal health and welfare have become increasingly common, and are often incorporated into quality assurance (QA) programmes. In a previous publication, we outlined the rationale for these standards, concerns that have been raised, and a framework that could be used as a tool direction for programme evaluation or as a tool to assist with programme development and review. In this study, this framework will be applied to evaluate four existing private standards and associated QA programmes.

Antimicrobial usage

Support for iNAP Database implementation

Collins, Á. et al.
DAFM & UCD CVERA

Ireland's National Action Plan on Antimicrobial Resistance 2017-2020 (iNAP) recognises the urgent and growing problem of antimicrobial resistance for human health worldwide. It aims to implement policies and actions to prevent, monitor and combat AMR across the health, agricultural and environmental sectors. Reducing the inappropriate use of antimicrobial medicines, as well as preventing the transmission of infections and disease, is vital to stop the development and spread of resistant microorganisms. Accurate farm-level antimicrobial usage estimates are only possible with accurate information about both farm-level antimicrobial usage and the population-at-risk. Currently, however, there is no single accurate measure of pig population in Ireland. The CVERA component of this project will aim to develop a pig population model in order to accurately estimate the number of pigs in commercial Irish pig herds.

European perspectives on efforts to reduce antimicrobial usage in food animal production

More, S.J.
UCD CVERA

Irish Veterinary Journal (in press)

New regulations on veterinary medicines and medicated feed will substantially influence antimicrobial prescribing and usage throughout Europe into the future. These regulations have been informed by a very large body of work, including the substantial progress towards reduced antimicrobial usage in food animal production in a number of member states of the European Union (EU). This paper seeks to summarise European perspectives on efforts to reduce antimicrobial usage in food animal production. Work within the EU is informed by the global action plan of the World Health Organization, which includes a strategic objective to optimise the use of antimicrobial medicines in human and animal health. There is ongoing measurement of trends in antimicrobial usage and resistance throughout the EU, and detailed information on strategies to reduce the need to use antimicrobials in food animal production. Substantial scientific progress has been made on the measurement of antimicrobial usage, including at herd-level, and on the objective assessment of farm biosecurity. In a number of EU member states, monitoring systems for usage are well-established, allowing benchmarking for veterinarians and farms, and monitoring of national and industry-level trends. Several countries have introduced restrictions on antimicrobial prescribing and usage, including strategies to limit conflicts of interest around antimicrobial prescribing and usage. Further, a broad range of measures are being used across member states to reduce the need for antimicrobial usage in food animal production, focusing both at farm level and nationally. Veterinarians play a central role in the reduction of antimicrobial usage in farm animals. Ireland's National Action Plan on Antimicrobial Resistance 2017–20 (iNAP) provides an overview of Ireland's commitment to the development and implementation of a holistic, cross-sectoral 'One Health' approach to the problem of antimicrobial resistance. The new regulations offer an important springboard for further progress, in order to preserve the efficacy of existing antimicrobials, which are a critical international resource.

An update on the use of national-level sales data to describe trends in intramammary antimicrobial usage on Irish dairy farms from 2015-2018

McAloon, C. et al.
UCD School of Veterinary Medicine

Antimicrobial usage data are needed both for benchmarking and to allow critical evaluation of usage patterns, both for domestic use and international comparison. Using sales data, More et al. (2017) presented detailed insights into intramammary antimicrobial usage in Ireland up to 2015. There have been many changes to the Irish dairy industry since 2015 with potential implications for antimicrobial usage, including legislation prohibiting blanket dry cow therapy, a major change in the demographic of the Irish dairy industry and increasing global concern (and action) with respect to AMR. The purpose of the current study is to update earlier work, describing trends in intramammary antimicrobial usage in the national Irish dairy industry during 2016-18.

Food safety & quality

The relationship between *Campylobacter* prevalence and key production and welfare indicators recorded in Irish broiler production

Collins, Á. et al.
DAFM & UCD CVERA

Preparation and consumption of chicken contaminated with *Campylobacter jejuni* is the leading cause of food-borne illness in Ireland and the EU. Reducing the level of *Campylobacter* infection at source is crucial to reducing the incidence of food-borne illness in humans. In the context of ‘One Health One Welfare’, this project proposes to examine associations between batch-level *Campylobacter* status of Irish broilers and key indicators of animal health, animal welfare and economic significance for the Irish broiler industry.

Foot and mouth disease

Engagement with the European Commission for the control of Foot-and-Mouth Disease via the EuFMDiS foot-and-mouth disease modelling project

Casey, M. et al.

UCD CVERA

In line with DAFM strategic objectives for safeguarding animal health and welfare and accessing international markets, the development of a national FMD model for Ireland would improve preparedness and optimise outbreak management strategies to ameliorate impacts on the agri-food industry. This project will serve as an introduction to the concept of modelling category A diseases for Ireland with a view to developing a more tailored model in the future. It will also promote positive engagement with EuFMD and contingency planning for category A diseases. The project will deliver data and assumptions to adapt the EuFMDiS national FMD model for Ireland.

Foot and mouth disease atmospheric dispersion system

Lambkin, K.[1], Hamilton, J.[1], McGrath, G.[2], Dando, P.[3], Draxler, R.[4]

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Advances in Science and Research 16, 113-117 (2019)

A decision support system to aid in the risk evaluation of airborne animal diseases was developed for Ireland. The system's primary objective is to assist in risk evaluation of the airborne spread of Foot and Mouth Disease (FMD). The operational system was developed by Met Éireann – the Irish Meteorological Service and CVERA (Centre for Veterinary Epidemiology and Risk Analysis), in co-operation with NOAA-ARL (National Oceanic and Atmospheric Administration – Air Resources Laboratory) and ECMWF (European Centre for Medium-Range Weather Forecasts). The infrastructure largely relies on the HYSPLIT dispersion model driven by both ECMWF meteorological forecasts for longer range simulations, and HARMONIE-AROME meteorological forecasts, a high resolution local area meteorological model, ideal for shorter range national emissions. Following on from previous work by the Bureau of Meteorology, Australia as well as the Australian Department of Agriculture, Fisheries and Forestry, further modifications were made to the HYSPLIT source code to improve the model's characterisation of the Foot and Mouth Disease virus. FMD is a highly infectious disease among cloven hoofed animals that can transmit via airborne means. Biological characteristics related to temperature, humidity, lifespan as well as atmospheric washout were all incorporated either through new or existing functionality of the dispersion model. Combining the model dispersion capabilities of HYSPLIT with a virus emission model and GIS mapping software with farmland zoning, the disease dispersion system becomes a powerful analysis and decision support tool. This airborne animal disease atmospheric dispersion system helps improve emergency preparedness, as well as aid confinement and eradication strategies for relevant Irish authorities, during a disease outbreak.

Improvement and documentation of CVERA's involvement in any potential Foot and Mouth outbreak in Ireland

Tratalos, J. et al.
UCD CVERA

Foot and Mouth Disease (FMD) is a highly contagious disease and the economic effects of an outbreak on the farming and rural communities, in particular, could be extremely serious. Ireland needs to continue to ensure its preparedness for a FMD outbreak. This project will consist of the development of a computer programme to calculate FMD virus production at a farm level during an outbreak. The output will be tested within the HYSPLIT atmospheric modelling tool to generate aerial plumes of FMD virus. The plumes will be overlayed over farm locations to assist targeted surveillance. The potential for automation of these procedures within a Python modelling framework will be investigated. This methodology will be integrated into CVERA's Standard Operating Procedures (SOP) in response to a notification of a possible FMD outbreak in Ireland.

Marine animal health

Can biosecurity and local network properties predict pathogen species richness in the salmonid industry?

Yatabe, T.[1], More, S.J.[2], Geoghegan, F.[3], McManus, C.[4], Hill, A.E.[5], Martínez-López, B.[1]

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PloS One 13, e0191680 (2018)

Salmonid farming in Ireland is mostly organic, which implies limited disease treatment options. This highlights the importance of biosecurity for preventing the introduction and spread of infectious agents. Similarly, the effect of local network properties on infection spread processes has rarely been evaluated. In this paper, we characterized the biosecurity of salmonid farms in Ireland using a survey, and then developed a score for benchmarking the disease risk of salmonid farms. The usefulness and validity of this score, together with farm indegree (dichotomized as ≤ 1 or > 1), were assessed through generalized Poisson regression models, in which the modeled outcome was pathogen richness, defined here as the number of different diseases affecting a farm during a year. Seawater salmon (SW salmon) farms had the highest biosecurity scores with a median (interquartile range) of 82.3 (5.4), followed by freshwater salmon (FW salmon) with 75.2 (8.2), and freshwater trout (FW trout) farms with 74.8 (4.5). For FW salmon and trout farms, the top ranked model (in terms of leave-one-out information criteria, looic) was the null model (looic = 46.1). For SW salmon farms, the best ranking model was the full model with both predictors and their interaction (looic = 33.3). Farms with a higher biosecurity score were associated with lower pathogen richness, and farms with indegree > 1 (i.e. more than one fish supplier) were associated with increased pathogen richness. The effect of the interaction between these variables was also important, showing an antagonistic effect. This would indicate that biosecurity effectiveness is achieved through a broader perspective on the subject, which includes a minimization in the number of suppliers and hence in the possibilities for infection to enter a farm. The work presented here could be used to elaborate indicators of a farm's disease risk based on its biosecurity score and indegree, to inform risk-based disease surveillance and control strategies for private and public stakeholders.

Data-driven network modelling of disease transmission using population movement data: Piscine myocarditis virus (PMCV) in the Irish farmed Atlantic salmon population

Yatabe, T. et al.

Center for Animal Disease Modeling and Surveillance (CADMS), Department of Medicine & Epidemiology, School Veterinary Medicine, University of California, Davis, California, USA

Earlier work has shown that the network of live fish movements in Ireland possesses characteristics that would facilitate infection spread. Cardiomyopathy syndrome (CMS) is a severe cardiac disease of Atlantic salmon caused by Piscine myocarditis virus (PMCV) that was first reported in Ireland in 2012. Here, we fitted a network-based stochastic infection spread model to estimate countrywide prevalence and evaluate mitigation strategies based on farm centrality measures that could have helped in preventing the spread of the agent. This information could inform prevention and control policies for this and other infectious agents in the future.

Schmallenberg virus

Hypothetical route of the introduction of Schmallenberg virus into Ireland using two complementary analyses

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Veterinary Record 182, 226 (2018)

Ireland lost its official freedom from Schmallenberg virus (SBV) in October 2012. The route of introduction is uncertain, with long-distance displacement of infected *Culicoides*, biting midges, by suitable wind flows considered to be the most likely source. The authors investigated the potential introduction of SBV into Ireland through a *Culicoides* incursion event in the summer of 2012. They conducted SBV serology on archived bovine sera to identify the prospective dispersal window, then used atmospheric dispersion modelling during periods around this window to identify environmental conditions the authors considered suitable for atmospheric dispersal of *Culicoides* from potential infected source locations across Southern England. The authors believe that there was one plausible window over the summer of 2012, on August 10-11, based on suitable meteorological conditions. They conclude that a potential long-range transportation event of *Culicoides* appears to have occurred successfully only once during the 2012 vector competent season. If these incursion events remain at a low frequency, meteorological modelling has the potential to contribute cost-effectively to the alert and response systems for vectorborne diseases in the future.

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The emergence and re-emergence of SBV in Ireland

Barrett, D. et al

DAFM

Schmallenberg virus (SBV) is a simbu serogroup Orthobunyavirus (family *Bunyaviridae*), which was first identified in Europe in August 2011, and the first case was in Ireland in October 2012. The virus is transmitted by a variety of

Culicoides species, and it was the first midge borne disease known to affect ruminants in Ireland. The PhD thesis has now been finalised, contributing substantially to our understanding of SBV in an Irish context. Most of this work has already been published, with one final paper in preparation, investigating the geographic distribution of exposure to Schmallenberg virus following its reappearance in Ireland during the autumn of 2016.

Transmissible spongiform encephalopathy (TSE)

Using an epidemiological framework and bovine spongiform encephalopathy investigation questionnaire to investigate suspect bovine spongiform encephalopathy cases: an example from a bovine spongiform encephalopathy case in Ireland in 2015

O'Connor, J.T.[1], Byrne, J.P.[1], More, S.J.[2], Blake, M.[3], McGrath, G.[2], Tratalos, J.A.[2], McElroy, M.C.[1], Kiernan, P.[1], Canty, M.J.[1], O'Brien-Lynch, C.[3], Griffin, J.M.[3]

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Veterinary Record 182, 168 (2018)

In several EU member states, bovine spongiform encephalopathy (BSE) cases have been identified in cattle born after the reinforced ban (BARB cases), for reasons that are not entirely clear. Epidemiological investigation of these cases has proved challenging. The European Food Safety Authority recently recommended the collection of a predefined set of epidemiological data from BSE suspects and confirmed BSE cases to aid future investigations. In this study, we present an epidemiological framework and BSE investigation questionnaire to aid the investigation of suspect BSE cases, and illustrate its application during the investigation of a BSE case in Ireland in 2015. It is recommended that the framework and questionnaire are used concurrently: the framework provides structure and focus, whereas the questionnaire (with 135 questions) aids data collection. The framework focuses on confirmation and discrimination, estimating the date and location of exposure, and determining the method/source of exposure. The BSE case in Ireland in 2015 was a BARB case born in 2010. It was identified with classical BSE at an authorised knackery as part of Ireland's targeted active surveillance programme for BSE. No definitive source of infection with the BSE agent could be attributed in this case.

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Other farmed ruminant health issues

Influenza D Virus in cattle, Ireland

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Emerging Infectious Diseases 24, 389-391 (2018)

We detected influenza D virus in 18 nasal swab samples from cattle in Ireland that were clinically diagnosed with respiratory disease. Specimens were obtained from archived samples received for routine diagnosis during 2014-2016. Sequencing showed that viruses from Ireland clustered with virus sequences obtained in Europe within the D/swine/OK/1334/2011 clade.

Culicoides dispersion model

McGrath, G. et al.

UCD CVERA

DAFM currently uses plume plots generated by Met Éireann using NOAA's (National Oceanic and Atmospheric Administration) HYSPLIT atmospheric dispersion model driven by European Centre for Medium-Range Weather Forecasts (ECMWF) weather forecasts to identify suitable weather conditions for the potential spread of Culicoides into Ireland. Culicoides are a potential host for Bluetongue virus. The forecasts from the model inform DAFM risk assessments, early warning surveillance and risk mitigation actions to reduce the impact of a potential incursion of Bluetongue into Ireland. This project will identify additional parameters for integration into the model to better simulate true dispersion potentials for Culicoides.

Liver fluke in Irish sheep: prevalence and associations with management practices and co-infection with rumen fluke

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Parasites & Vectors 12, 525 (2019)

The present study aimed to identify the national prevalence of *Fasciola hepatica* in Irish sheep and to conduct a risk analysis assessment based on management and treatment practices in participating flocks. Also, co-infection with rumen fluke was quantified and its association with liver fluke and management practices was assessed. A total of 305 sheep flocks were selected ensuring even national representation of the sheep population. Participating farms were asked to complete a survey questionnaire on farm management practices and submit faecal samples during the winter of 2014-2015. Pooled faecal samples were analysed for the presence of *F. hepatica* and co-infection with rumen fluke. Apparent and true prevalence were calculated, additionally, the rate of co-infection with rumen fluke was also obtained. Correlation and regression analyses were used for assessing associations between management practices, liver fluke infection and co-infection with rumen fluke. The national true prevalence of *F. hepatica* was 50.4% (n = 305). Regional prevalence varied from 41% in the east to 52% in the south. Co-infection with rumen fluke was observed in 40% of the studied population and correlated with increased *F. hepatica* egg counts (OR = 2.9; $P \leq 0.001$). Predominant breeds were Suffolk, Texel and Horned Mountain breeds. Beef cattle were the most frequent type of other livestock present on farms and mixed species grazing was frequently reported (73%). More than half of the flocks reported a mid-to-late lambing period (March-April). Use of mountain land for grazing was of 32%. Flukicides were most commonly used twice over the autumn-winter period. Regression analyses highlighted significant association of *F. hepatica* status, with the presence of other livestock on farm, frequency of flukicides used during the winter and clinical presentation of liver fluke. A significant increase in eggs per gram of faeces was observed in Charollais sheep in comparison with all other breeds. Co-infection with *F. hepatica* and *Calicophoron daubneyi* was also significantly associated with the presence of other livestock on the farm, type of flukicide used and clinical fasciolosis. The present study provides up-to-date information on the prevalence of *F. hepatica* in Irish sheep and adds insight to the epidemiology of the disease. These findings will be useful for designing new holistic control measures for *F. hepatica* infection.

Risk factors associated with exposure to bovine respiratory disease pathogens during the peri-weaning period in dairy bull calves

Murray, G.M.[1], More, S.J.[2], Clegg, T.A.[2], Earley, B.[3], O'Neill, R.G.[1], Johnston, D.[3], Gilmore, J.[4], Nosov, M.[4], McElroy, M.C.[1], Inzana, T.J.[5], Cassidy, J.P.[6]

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BMC Veterinary Research 14, 53 (2018)

Bovine respiratory disease (BRD) remains among the leading causes of death of cattle internationally. The objective of this study was to identify risk factors associated with exposure to BRD pathogens during the peri-weaning period (day (d)-14 to d 14 relative to weaning at 0) in dairy bull calves using serological responses to these pathogens as surrogate markers of exposure. Clinically normal Holstein-Friesian and Jersey breed bull calves (*n* = 72) were group housed in 4 pens using a factorial design with calves of different breeds and planes of nutrition in each pen. Intrinsic, management and clinical data were collected during the pre-weaning (d – 56 to d – 14) period. Calves were gradually weaned over 14 days (d – 14 to d 0). Serological analysis for antibodies against key BRD pathogens (BRSV, BPI3V, BHV-1, BHV-4, BCoV, BVDV and *H. somni*) was undertaken at d – 14 and d 14. Linear regression models (for BVDV, BPI3V, BHV-1, BHV-4, BCoV and *H. somni*) and a single mixed effect random variable model (for BRSV) were used to identify risk factors for changes in antibody levels to these pathogens. BRSV was the only pathogen which demonstrated clustering by pen. Jersey calves experienced significantly lower changes in BVDV S/P than Holstein-Friesian calves. Animals with a high maximum respiratory score (≥8) recorded significant increases in *H. somni* S/P during the peri-weaning period when compared to those with respiratory scores of ≤3. Haptoglobin levels of between 1.32 and 1.60 mg/ml at d – 14 were significantly associated with decreases in BHV-1 S/N during the peri-weaning period. Higher BVDV S/P ratios at d – 14 were significantly correlated with increased changes in serological responses to BHV-4 over the peri-weaning period. Haptoglobin may have potential as a predictor of exposure to BHV-1. BRSV would appear to play a more significant role at the 'group' rather than 'individual animal' level. The significant associations between the pre-weaning levels of antibodies to certain BRD pathogens and changes in the levels of antibodies to the various pathogens during the peri-weaning period may reflect a cohort of possibly genetically linked 'better responders' among the study population.

Antibodies to *Coxiella burnetii* in Irish bulk tank milk samples

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Veterinary Record 182, 550 (2018)

Coxiella burnetii is the aetiological agent of Q fever, a zoonotic disease with a worldwide distribution whose main reservoirs are goats, sheep and cattle. In ruminants, infection can cause abortion and reproductive problems, with large numbers of infectious organisms shed at parturition, in milk and in urine and faeces. Infection of humans occurs mainly via the respiratory route, with airborne spread possible beyond the boundaries of the infected farm. In Ireland, there were six recorded human cases of Q fever in humans in 2016, but it is reasonable to assume that the true human incidence is considerably higher. This paper seeks to obtain a more accurate estimate of the prevalence of antibodies to *C. burnetii* in Irish dairy herds.

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Science-policy interface

Perspectives from the science-policy interface in animal health and welfare

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Frontiers in Veterinary Science 6, 382 (2019)

The aim of this paper is to present scientific perspectives from the science-policy interface in animal health and welfare, with an emphasis on factors critical to scientific effectiveness. While there is broad acceptance of the value of scientific information to inform policy-making, interactions at the science-policy interface are not without difficulties. The literature highlights the need for scientists to build policy relevance to the research focus from the outset, to engage with policy-makers and other stakeholders throughout, to use platforms to facilitate science-policy dialogue, and to disseminate research findings appropriately. In the author's experience, there are a range of factors linked with effectiveness at the science-policy interface in animal health and welfare including a passion for public interest research, scientific independence, a commitment to scientific quality and openness, the opportunities afforded from partnership and collaboration, and an interest in strategic thinking and systems change. In an increasingly complex and rapidly changing world, an objective evidence base for policy decision-making is more important than ever. There is a need for particular attention to the value of collaboration between the natural and social sciences, a recognition among scientists and policy-makers that science is not value-free, the importance of effective communications, and the need to assess and communicate uncertainty. Further, there are particular challenges with science conducted in support of policy development for industry. It is hoped that this paper will stimulate and contribute to discussion and debate, both among scientists and between scientists and policy-makers, to increase scientific effectiveness at the science-policy interface in animal health and welfare.

Miscellaneous

Development of a working model for predicting and identifying the locations of contaminated farms following a nuclear accident event

McGrath, G. et al.
UCD CVERA

CVERA, in conjunction with the Office of Radiation Protection and Environmental Monitoring – Environmental Protection Agency (ORM - EPA), Met Éireann and the Department of Agriculture Food and the Marine, will create a model for defining the extent and severity of contamination of Irish farm land, both during and after a nuclear accident scenario in the United Kingdom or continental Europe. An operational system will be developed that will assign a risk category to farms based on their calculated exposure to radiation in the event of a nuclear accident. Knowing where areas of negligible risk are would allow for an uninterrupted supply of farming produce to the general public and for export. Having a system such as this in place would offer a degree of security in what would be a period of uncertainly in consumer confidence in agricultural produce.

VKORC1 sequence variants associated with resistance to anticoagulant rodenticides in Irish populations of *Rattus norvegicus* and *Mus musculus domesticus*

Mooney, J.[1], Lynch, M.R.[2], Prescott, C.V.[3], Clegg, T.[4], Loughlin, M.[5], Hannon, B.[6], Moore, C.[7], Faulkner, R.[7]
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Scientific Reports 8, 4535 (2018)

While resistance to anticoagulant rodenticides is known to occur in many European populations of Norway rat and house mouse, to-date no data is available on the occurrence in Ireland of such resistance. No genetic evidence for the occurrence of resistance was found in 65 Norway rat samples analysed, indicative of an absence, or low prevalence, of resistance in rats in at least the Eastern region of the island of Ireland. The presence of two of the most commonly found amino acid substitutions Leu128Ser and Tyr139Cys associated with house mouse resistance to anticoagulant rodenticides was confirmed. The occurrence of two such mutations is indicative of the occurrence of resistance to anticoagulant rodenticides in house mice in the Eastern region of the island of Ireland.

Validation of a spatial liver fluke model under field conditions in Ireland

Naranjo Lucena, A.[1], Munita Corbalán, M.P.[2], Martínez-Ibeas, A.M.[2], McGrath, G.[3], Sayers, R.[2], Mulcahy, G.[3], Zintl, A.[3]

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Geospatial Health 13, 641 (2018)

Fasciola hepatica is the causative agent of fasciolosis, a global disease of a wide range of mammals, particularly sheep and cattle. Liver fluke infection causes annual losses estimated at around €2.5 billion to livestock and food industries worldwide. Various models have been developed to define risk factors and predict exposure to this liver fluke in ruminants in European countries, most of them based exclusively on data from dairy herds. The aim of this study was to validate a published theoretical baseline risk map of liver fluke exposure and cluster maps in Ireland, by including further explanatory variables and additional herd types that are spatially more widespread. Three approaches were employed: i) comparison of predicted and actual exposure; ii) comparison of cluster distribution of hotspots and coldspots; and iii) development of a new model to compare predicted spatial distribution and risk factors. Based on new survey data, the published baseline predictive map was found to have a sensitivity of 94.7%, a specificity of 5%, a positive predictive value of 60% and a negative predictive value of 38.2%. In agreement with the original model, our validation highlighted temperature and rainfall among the main risk factors. In addition, we identified vegetation indices as important risk factors. Both the previously published and our new model predict that exposure to *Fasciola* is higher in the western parts of Ireland. However, foci of high probability do not match completely, nor do the location of clusters of hotspots and coldspots.

Spatial patterns of *Fasciola hepatica* and *Calicophoron daubneyi* infections in ruminants in Ireland and modelling of *C. daubneyi* infection

Naranjo-Lucena, A.[1], Munita Corbalán, M.P.[2], Martínez-Ibeas, A.M.[2], McGrath, G.[3], Murray, G.[4], Casey, M.[4], Good, B.[5], Sayers, R.[2], Mulcahy, G.[1], Zintl, A.[1]

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Parasites & Vectors 11, 531 (2018)

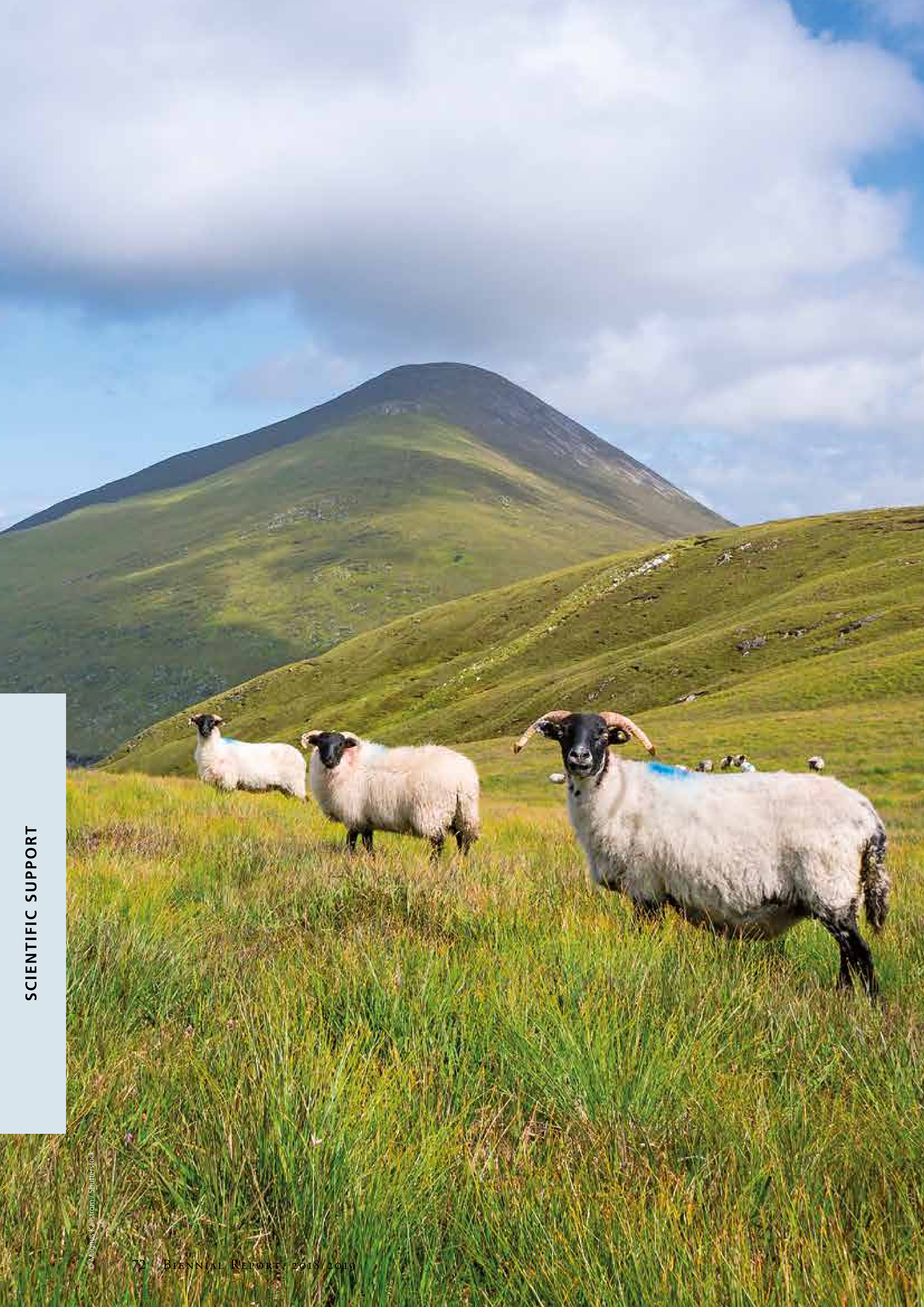
Fasciola hepatica has always represented a threat to Irish livestock because the Irish climate is highly suitable for the main local intermediate host of the parasite, the snail *Galba truncatula*. The recent clinical emergence of infections due to *Calicophoron daubneyi* has raised the question of whether the two parasites, which share a niche during part of their life-cycles, interact in some way. Here, we used geographical information systems (GIS) to analyse the distribution of both parasites in cattle and sheep. We also developed the first predictive model of paramphistomosis in Ireland. Our results indicated that, in cattle, liver fluke infection is less common than rumen fluke infection and does not exhibit the same seasonal fluctuations. Overall, we found that cattle had a higher likelihood of being infected with rumen fluke than sheep (OR = 3.134, $P < 0.01$). In addition, infection with one parasite increased the odds of infection with the other in both host species. Rumen fluke in cattle showed the highest spatial density of infection. Environmental variables such as soil drainage, land cover and habitat appeared to be the most important risk factors for *C. daubneyi* infection, followed by rainfall and vegetation. Overall the risk of infection with this parasite was predicted to be higher in the west of the country. This study shows differences between the infection rates and spatial patterns of bovine and ovine infections

with *F. hepatica* and *C. daubneyi* in Ireland. Whether the reasons for this are due to susceptibility, exposure and/or management factors is yet to be determined. Furthermore, the rumen fluke model indicates distinct risk factors and predicted distribution to those of *F. hepatica*, suggesting potential biological differences between both parasite species.

Mapping wild bird avian influenza surveillance results

Tratalos, J. et al.
UCD CVERA

Avian influenza is a contagious and often fatal viral disease of birds which, depending on severity, can be range from low to highly pathogenic. An outbreak of the disease could have a serious impact on the poultry industry in Ireland. Wild birds, particularly wild migratory water birds, are the primary reservoir of avian influenza viruses. This study will generate maps of wild bird avian influenza surveillance results and will inform contingency planning for emergency response to disease.



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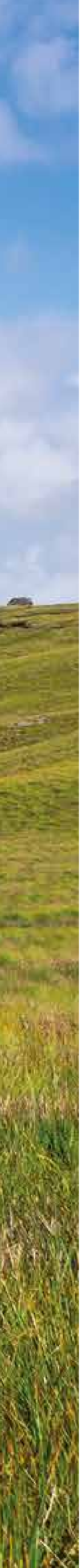

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Scientific support

Scientific support

CVERA works to generate scientific information in support of national policy decision-making. This work is conducted in two ways, either as:

- defined *scientific projects* (as outlined in earlier sections of this Biennial Report [Bovine tuberculosis; Non-regulatory cattle health issues; Other animal health and welfare issues]), or
- as more-general *scientific support.*

Each accounts for approximately 50% of available resources.

CVERA provides scientific support to both *ad hoc* or ongoing activities, and to a range of national bodies including the Department of Agriculture, Food and the Marine, University College Dublin and Animal Health Ireland. In each case, the work draws on expertise within CVERA in epidemiology, statistics, geographic information systems and database maintenance and interrogation.

The following provide a broad, non-exhaustive overview of scientific support provided by CVERA during 2018 and 2019.

Epidemiological support

Simon More

Department of Agriculture, Food and the Marine

- Member, Scientific Advisory Committee on Animal Health and Welfare
- Member, TB Forum
- Member, iNAP Animal Health Implementation Committee
- Member, Animal Health Surveillance Steering Group
- Member, TB/BR North/South Working Group
- Member, CVERA management board
- Epidemiological support on a range of issues including:
    - National animal disease surveillance design, including a national bluetongue survey to substantiate freedom
    - Measurement of antimicrobial usage in farmed animals
    - Characterising animal movement: implications for national disease control

University College Dublin

- Associate Dean for Research, Innovation and Impact within the UCD School of Veterinary Medicine
    - Chair, Research, Innovation and Impact Committee, UCD School of Veterinary Medicine
    - Member, Research, Innovation and Impact Committee, UCD College of Health and Agricultural Sciences
    - Member, Research, Innovation and Impact Group, University College Dublin
    - Member, Senior Management Team, UCD School of Veterinary Medicine
    - Member, Athena SWAN action team, UCD School of Veterinary Medicine
- Teaching
    - Undergraduate, including Agricultural Science (ANSC30130), Veterinary Medicine (VETS30170, VETS30290) and Medicine (MDSA10210)
    - Postgraduate, including Agricultural Science (AESC40020) and Dairy Herd Health (VETS40180)

- Postgraduate supervision or support
    - Finalised during 2018/19: Inma Aznar (PhD Wageningen) [bTB epidemiology], Damien Barrett (PhD) [Schmallenberg epidemiology], Ger Murray (PhD) [bovine respiratory disease], Fiona Reardon (MVSc) [BVD epidemiology], Tadaishi Yatabe (PhD UC Davis) [fish disease epidemiology], Jarlath O'Connor (DGov) [bovine tuberculosis]
    - Ongoing: Jonas Brock (PhD Leipzig University) [infectious bovine rhinotracheitis], Ann Barber (PhD Wageningen University) [bovine tuberculosis], Annika van Roon (PhD Utrecht University) [tools for confidence of freedom from infection], Lisa Bradford (ECVPH) [epidemiology], Joana Pessoa (ECVPH) [epidemiology], Áine Collins (ECVPH) [epidemiology]

Other

- Presentation to the Oireachtas Joint Committee on Agriculture, Food and the Marine
- Animal Health Ireland
    - Chair of the Technical Work Group, member of the Implementation Group, Johne's disease
    - Chair of the Technical Work Group, member of the Implementation Group, CellCheck programme
    - Provision of scientific support to AHI on issues relating to the BVD, Johne's disease, CellCheck and IBR programmes
- European Food Safety Authority
    - Chair of the Scientific Committee (SC)
    - Chair of the MUST-B (multiple stressors on honey bee colony health) working group
    - Member of the African Swine Fever (ASF) working group
- General scientific community
    - Editorial Advisory Board, *EFSA Journal*
    - Scientific Advisory Board, *Preventive Veterinary Medicine*
    - Deputy Editor, *Irish Veterinary Journal*
    - Independent referee for a number of international peer reviewed journals
    - Thesis examination (MVSc, PhD, *Doctor Medicinae Veterinariae*), several universities
    - Member, Scientific Committee, 7th International Conference on *Mycobacterium bovis* (*M. bovis* 2020)

Statistical support

Jamie Madden

Department of Agriculture, Food and the Marine

- Statistical support on a range of issues including:
    - National bTB eradication programme
    - Development of a herd bTB breakdown file for use:
        - by DAFM's One Health Unit
        - for annual bTB incidence maps
        - for spatio-temporal modelling for bTB projects

University College Dublin

- Providing statistical support for a range of ongoing studies for CVERA related projects. In addition to, providing support for papers which are close to submission:
    - Spatial and network characteristics of Irish cattle movements
    - Kilkenny badger vaccination project

Other

- Independent referee for a number of international peer reviewed papers

Geographic Information Systems (GIS) support

Guy McGrath & Daniel Collins

Department of Agriculture, Food and the Marine

- Wildlife Administration Unit
  DAFM's Wildlife Administration Unit (WAU) has had responsibility for the implementation of the Department's wildlife strategy for bovine tuberculosis since its foundation in 2002. The strategy is implemented under licence from, and in co-operation with, National Parks and Wildlife Service (NPWS). CVERA provides support to the WAU vaccination and control elements of the TB eradication programme. CVERA will continue to provide:
    - Daily approvals and monthly/yearly reports for vaccine tile turnover and control programme
    - Issue of permits for removals in vaccine areas
    - End of year progress maps for each DVO
    - TB quarterly maps
    - Area treated calculations are submitted on a regular basis in compliance with NPWS
    - Resources for regional offices and problem areas
    - WAU annual calculations
    - Density metric data
    - Analysis of historic badger removal data in the Cork Four Area Project
    - Forest harvesting setts
- GIS support for a range of studies, including:
    - BVD "spider" map
    - Land fragmentation analysis of farms outside of DVO of origin
    - BSE background data extraction
    - Regional Laboratory Report
    - Data provision to laboratories
    - Maps of marts and facilities in border areas

University College Dublin

- GIS support for a range of studies, including:
    - BVD clustering assistance for final year project
    - Intramammary antibiotic usage

Animal Health Ireland

- GIS support for a range of studies, including:
    - Monthly BVD maps
    - All-island BVD maps

Other

- GIS support for a range of studies, including:
    - Meteorological server
    - Annual processing of Land Parcel Identification
    - Avian Influenza - European submissions (EFSA)
    - Shannon Scheme ecological report

Database and computer programming support

Jamie Tratalos

Department of Agriculture, Food and the Marine

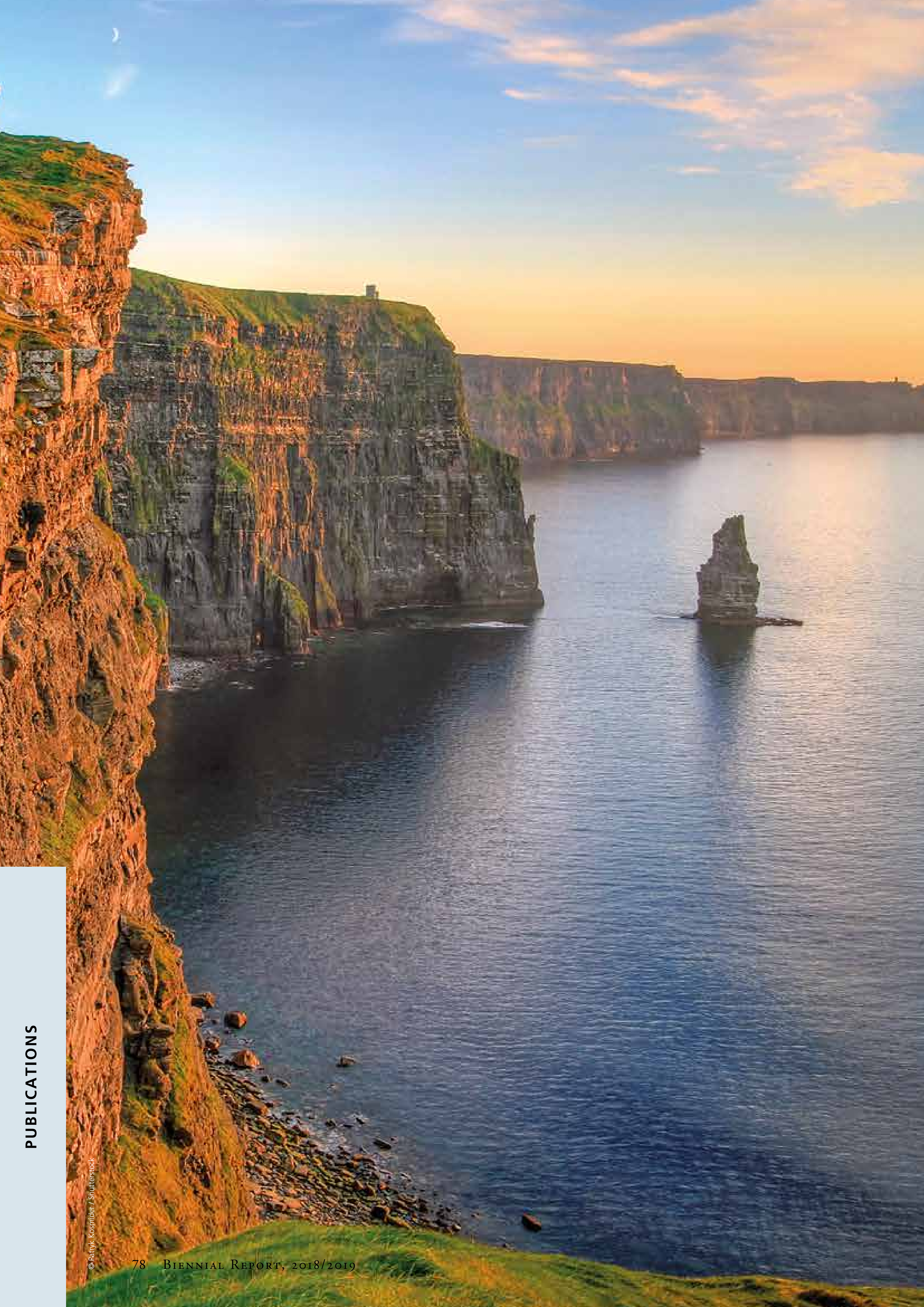
- AIM Bovine Statistics Report 2017 & 2018
- Annual Bluetongue freedom from disease analysis
- Calculation of farm level TCID50 (Tissue Culture Infectious Dose) per m3 for Foot and Mouth disease
- Provision of datasets and summary statistics for EuFMDiS Foot and Mouth Modelling Tool
- Provision of bovine movement datasets for use in a variety of projects
- Creation of herd and animal level TB datasets for use by CVERA staff
- Technical and analytical support to the DAFM abattoir surveillance group

University College Dublin

- Modification of testing database to provide updated test result criteria for Gamma Interferon tests

Other

- Database support for a range of studies, including:
    - Development of SQL data bases to ensure that CVERA is in compliance with national Data Protection legislation and that data is readily available in standardised formats for analysis by CVERA staff



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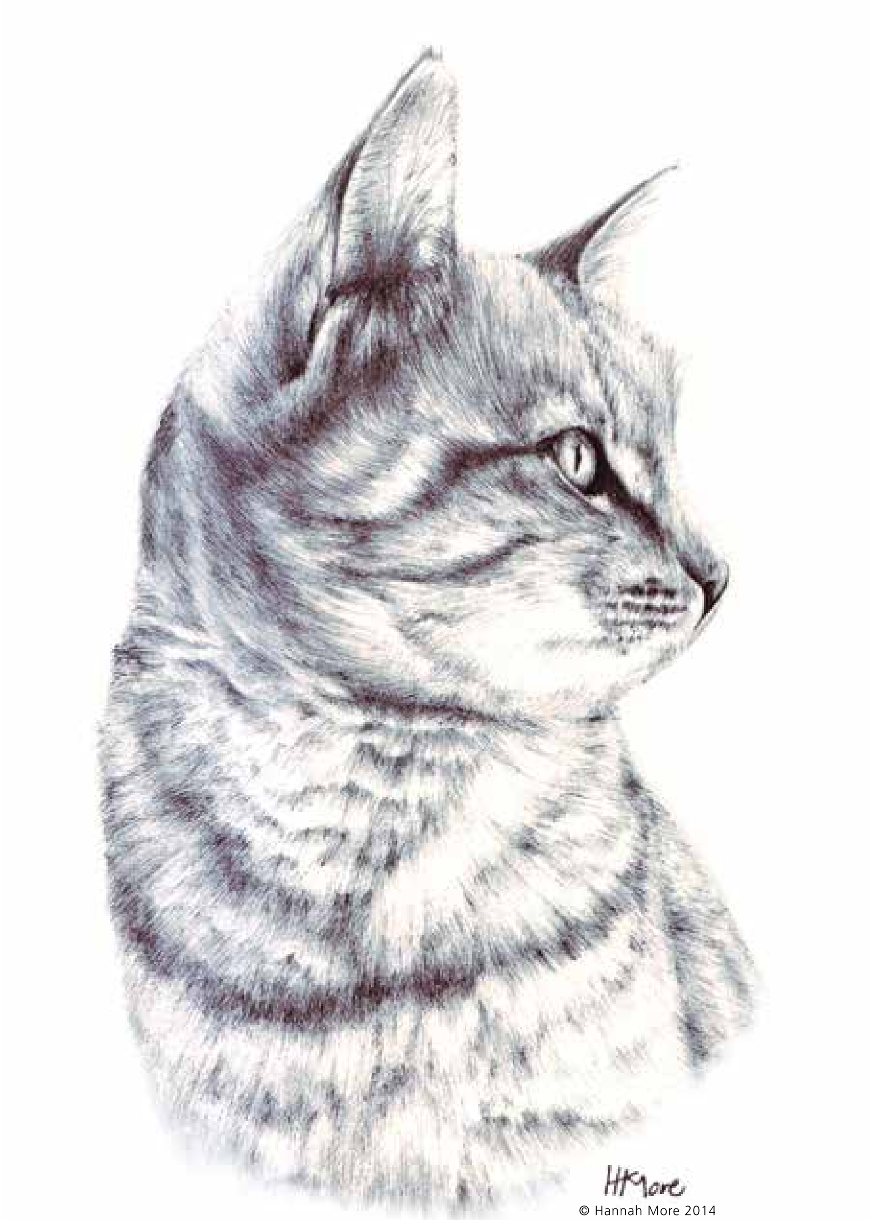

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Publications

During 2018 - 2019

Peer reviewed papers & book chapters

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Scientific opinions

S.J. More [UCD CVERA] with other members of the Panel on Animal Health and Welfare (AHAW) and the Scientific Committee (SC) of the European Food Safety Authority [EFSA]

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ISBN: 978-1-910963-43-2

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