



## AwardDetails

### Joint estimation of epidemiological and genetic processes for Mycobacterium bovis transmission dynamics in cattle and badgers

Reference	BB/L010569/1
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Department	College of Medical, Veterinary, Life Sci
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## Abstract

Quantifying the transmission dynamics of multi-host pathogens is challenging, especially when sampling is biased. An important example of this is Mycobacterium bovis, the causative agent of bovine TB (bTB) an important disease of British and Irish cattle. M. bovis circulates in the badger and cattle populations and is currently expanding rapidly in GB. While it is well known that persistence of bTB in cattle is spatially localised, the critical question of how these spatial 'patches' are spread and maintained and the role badgers play are as yet unresolved questions. Here, we propose to combine whole genome sequencing (WGS) technology with detailed population data on both hosts to shed new light onto this problem. To address this question, we shall use the exceptional datasets available to integrate analyses across two organisational scales - the 'patch' scale of local persistence and spread and the transmission at the individual level within cattle herds and badger social groups. First, the natural spatial scale at which M. bovis is circulating shall be explored, using community structure algorithms from social network analysis to parse densely sampled phylogenetic trees by the most relevant clade structures. Second, the persistence and spread of bTB at the cattle herd and badger social group scale shall be investigated by analysing detailed life history and infection data. Mathematical models will be used to infer parameter distributions using Bayesian approaches; using methods that have already been used to study a number of important infectious diseases, including bTB. As the integration of genetic and epidemiological data ('phylodynamics') is as yet little applied to bacterial pathogens, not only shall this project generate important insights into bTB epidemiology, it shall also be a useful exemplar to others interested in mycobacterial phylodynamics in general.

## Summary

The control and eradication of infectious diseases can be difficult for pathogens that are able to persist in multiple host species. This is the case for bovine tuberculosis (bTB), a disease primarily affecting cattle but also found in a number of wildlife species; in Britain and Ireland, the most important of these is the Eurasian badger (*Meles meles*). While Ireland has had a persistent bTB problem in cattle, by the 1970's bTB had been almost eradicated from Great Britain but since then there has been a dramatically re-emerging disease in cattle. bTB is a zoonosis with implications for both human and animal health, though chronic cases of either in Britain and Ireland are few. Control of bTB also places a severe strain on individual farmers, the farming industry and government, with a projected cost in England and Wales alone of over £1bn over the next decade. While it has long been suspected that badgers are involved, research efforts to date have not determined the extent to which badgers are responsible for eradicating bTB from cattle, and this topic is the subject of great social and political controversy. One of the most important developments in epidemiology of the last few decades has been the increased use of 'genetic fingerprinting' to identify patterns of disease spread. Until recently, this has largely been done using only a small number of selected regions in the genome. While this kind of "genetic fingerprinting" has been very useful and shows that cattle and badgers in the same region are usually infected by the same bTB strain, the fingerprints are far from unique: many cattle and many badgers share the same type, making it impossible to determine who infected whom. In this project, we will take advantage of novel technology making it feasible and affordable to sequence the entire *M. bovis* genome for large numbers of samples. Because the bacterium occasionally makes mistakes while replicating its genome, new mutations constantly arise not seen using traditional fingerprinting methods but with the new technology creating a much more unique and discriminatory genetic fingerprint of transmission. Using samples collected over decades from cattle and badgers in Great Britain and Northern Ireland, we will sequence the genomes of hundreds of isolates to genetically track the spread of the pathogen and to test whether it is predominantly maintained in cattle, in badgers, or both. The unique opportunity exploited in this proposal is the availability of extraordinarily dense sampling of cattle and badgers infection together with entire life histories of individual cattle, including movement to other farms and whether it became infected with bTB at some point of its life. This creates an exceptional resource, allowing us to compare our very detailed understanding of contacts between cattle and between herds with the genetic fingerprint information. Based on this information, we will use mathematical models linked directly to statistical inference methods to simulate how the infection may have spread through cattle populations in Britain and Ireland and how it may have genetically changed in the process. This will be done under various different assumptions about the multiple possible sources and mechanisms of infection. By comparing our simulated results to the actual observations (e.g. the number of infected cattle and the type of bTB they carry, etc), we will gain unprecedented insight into the drivers for the spread of the disease and what may prevent its current control.

## Impact Summary

Government stakeholders. Bovine tuberculosis (bTB) places a significant burden on national economies in Britain and Ireland with an estimated future cost of £1 billion over the next ten years. New insights or approaches generated by this project therefore have the potential to make a direct economic impact if they affect government policy and, in the long term, translate into more effective control strategies. In addition to monetary costs, the question of how to best control bTB, and in particular the use of badger culling, has become a hugely divisive, political issue. Any information that would help to place control strategies on more a science- and evidence-based footing, should therefore be valuable to policy makers. Generally, benefits from this project to the public sector may include I) insights into mechanisms of persistence and spread of the disease; II) Risk factors influencing the distribution, size and re-occurrence of bTB outbreaks on farms; III) evaluation of new molecular sequencing technology that could be incorporated into future diagnostic and control programs IV) Identify likely mechanisms and ranges of spread of high incidence areas for bTB V) Guidelines for bTB control, especially in terms of identifying methods to spatially target control and determine the extent of control required (both geographically, by species and by proportion of population) V) Identification of unrecognised knowledge gaps and research priorities. Cattle farming industry. Although there is legal compensation for cattle slaughtered as a result of testing positive for bTB, this covers only a fraction of the true cost, with a significant burden placed on farmers via the imposition of movement restrictions and the cost and effort associated with the multiple whole herd tests while the outbreak is being eradicated. This project will address long-standing questions about bTB epidemiology, persistence mechanisms and herd risk factors. Where answers to these questions can be used to improve management and control strategies, either through government policy or self-guided action, they will result in tangible benefits to the livestock industry. Wildlife conservation. The debate over the value of badger culling is an ongoing one, with sharply divided opinions on both sides, however it is currently considered one of the most important options for control of bTB. Better understanding of the role of badgers in the persistence of bTB will result in, at the very least, a more efficient approach to culling and/or provide better insight into the possible uses for vaccination. Wider public. A large part of the public is generally familiar with the issues surrounding bTB, the cost it places on tax payers and farming communities and the debate about whether badger culling is a defensible control strategy on both practical and ethical grounds. By providing objective scientific information about some of the underlying processes, this project therefore has the potential to help shape public opinion on these issues. We would also hope that by demonstrating the value of using novel science and technology tools to answer questions of significant public interest, this work could play a part in highlighting the benefits of research, and the use of public

funds, to society. Academic Impact. For expected academic impact, see 'Academic beneficiaries'

Committee	<a href="#">Research Committee A (Animal disease, health and welfare)</a>
Research Topics	Animal Health, Microbiology
Research Priority	X – Research Priority information not available
Research Initiative	X - not in an Initiative
Funding Scheme	X – not Funded via a specific Funding Scheme