Title	Understanding and managing bTB risk: Perspectives from Ireland
Authors(s)	More, Simon John, Good, Margaret
Publication date	2015-04-17
Publication information	More, Simon John, and Margaret Good. "Understanding and Managing bTB Risk: Perspectives from Ireland" 176, no. 3–4 (April 17, 2015).
Publisher	Elsevier
Item record/more information	http://hdl.handle.net/10197/7570
Publisher's version (DOI)	10.1016/j.vetmic.2015.01.026

Veterinary Microbiology 176 (2015) 209–218

Contents lists available at ScienceDirect

Veterinary Microbiology

journal homepage: www.elsevier.com/locate/vetmic

Review

Understanding and managing bTB risk: Perspectives from Ireland

Simon J. More [a,*], Margaret Good [b]

[a] UCD Centre for Veterinary Epidemiology and Risk Analysis, University College Dublin, Belfield, Dublin 4, Ireland
[b] Department of Agriculture, Food and the Marine, Kildare St, Dublin 2, Ireland

ARTICLE INFO

Article history:
Received 26 August 2014
Received in revised form 27 January 2015
Accepted 31 January 2015

Keywords:
Bovine tuberculosis
Ireland
Science
Policy
Risk
Persistence

ABSTRACT

There is substantial variation in herd risk for bovine tuberculosis (bTB) in Ireland, with most herds playing little to no role in the ongoing endemic. In infected areas, bTB persistence (affecting one or a group of herds) is a key feature of the infection. In this paper, we present our current understanding and management of bTB risk in Ireland, based on a detailed review of research and policy. There is close interaction between science and policy in Ireland, seeking both to understand and effectively manage bTB risk. Detailed research on bTB persistence is presented, including current understanding of the relative importance of different infection sources, which can include residual infection in cattle and/or re-infection, either from local sources or following cattle introduction. In recent years, there have been three primary drivers for policy change, including scientific advances, ongoing improvements to programme supports, and ongoing programme review. In this review, three key future programme challenges are identified. Although good progress is being made, eradication has not yet been achieved. Firstly, a key question concerns the additional effort that will be required, to move towards final eradication. Secondly, a percentage of non-infected animals are falsely positive to current testing methods. This is an ongoing challenge, given the imperfect specificity of test methods but will become more so, as the positive predictive value falls with reducing bTB prevalence. Finally, there is a need to re-engage with the farming community, so that they play a much greater role in programme ownership.

Contents

* Corresponding author. Tel.: +353 1 716 6071; fax: +353 1 716 6047.
E-mail address: simon.more@ucd.ie (S.J. More).

http://dx.doi.org/10.1016/j.vetmic.2015.01.026
0378-1135/

1. Introduction

There is substantial variation in herd risk for bovine tuberculosis (bTB) in Ireland, with most herds playing little to no role in the ongoing endemic. During 2003–2012, there were 4391 herds (3.7% of circa 120,000 extant herds) that had experienced ≥2 high risk breakdowns (1064 (0.9%) ≥3, 263 (0.2%) ≥4 and 52 (0.04%) ≥5), with a high risk breakdown defined as a period of herd restriction during which ≥2 infected animals were identified, either by field or abattoir surveillance. In general, outbreaks present as spatio-temporal clusters in defined localities. Local 'hot spots', where long-lasting clearance has proved difficult, have been a key feature of bTB in Ireland.

In this paper, we present our current understanding and management of bTB risk in Ireland, based on a detailed review of research and policy. We also consider reasons for bTB persistence, relevant policy responses, a critical review of national progress towards eradication, future challenges and additional thoughts.

2. Linking science and policy

In Ireland, science and policy are closely linked (More and Good, 2006), with scientists addressing the *what* (What are the key factors that influence bTB risk, locally, in herds, among animals?) and the *why* (What is the biological basis behind the observations?) and policy-makers considering the *how* (How are observed risks best managed?). Three research groups (the Centre for Veterinary Epidemiology and Risk Analysis, the TB Diagnostics and Immunology Research Centre, and the Badger Vaccine Project) have made substantial contributions to policy development since the late 1980s (Sheridan, 2011). There are regular meetings, both formal and informal, between scientists and policy-makers, focusing on both the broader picture (strategic research direction, project and personnel management, research output, external linkages) and on details relevant to specific projects. In Ireland, there has generally been little input from industry and other stakeholders on issues relating to strategic research direction other than expressing a desire that any programme modifications would be supported by research evidence.

3. Understanding bTB risk

In this section, we focus on two related, but distinct, issues:

- Section 3.1 considers herd-level risk factors for bTB presence (whether a herd is test positive or not at a point in time), and
- Section 3.2 on reasons for bTB persistence (the ongoing or repeated presence of bTB in a herd or locality despite control efforts).

3.1. Herd-level risk factors for bTB presence

Extensive research has been conducted on herd-level risk factors for bTB in Ireland. Over a broad range of studies, three factors have consistently placed herds at greatest risk of being diagnosed with bTB, namely herd size, location (including bTB prevalence in the area) and bTB history.

3.1.1. Herd size

bTB risk increases with herd size, for reasons that are not entirely understood. Increasing herd size may increase opportunity for exposure, both within the herd and from neighbouring herds (Griffin et al., 1996; White et al., 2013). In addition, herd-level specificity will decrease as the number of individuals being tested within each herd increases (Martin et al., 1992).

3.1.2. Herd location

bTB risk is also associated with herd location, with area-level prevalence and with infection in contiguous herds, leading to the spatial clustering observed. bTB is more likely to occur in groups of herds, rather than in isolation, leading to local persistence of infection. This is discussed in detail later.

3.1.3. Herd bTB history

Finally, many studies have highlighted the impact of bTB history on future risk (Olea-Popelka et al., 2004; Wolfe et al., 2009; Clegg et al., 2011b, 2013; Good et al., 2011; Gallagher et al., 2013). Olea-Popelka et al. (2004) first investigated this issue in detail, using a retrospective cohort study of Irish herds with ('exposed') and without

('non-exposed') bTB in 1995. Exposed herds were categorized into five increasing exposure-severity classes, based on the total number of standard SICTT (single intradermal comparative tuberculin test) reactors detected during the breakdown. Focusing on the hazard of a future multiple standard reactor breakdown, and compared to non-exposed herds, the hazard ratios ranged from 1.6 for exposed herds with only 1 standard reactor up to 2.9 in exposed herds with 8 or more standard reactors during the 1995 restriction. Thus, the hazard of a future breakdown was clearly linked to exposure-severity class. Presumptive bTB lesions in reactor cattle were not predictive of future breakdown hazard having controlled for other factors.

Several recent studies have taken this issue one step further, seeking to understand the longer term significance of past bTB history. In other words, will future bTB risk be influenced by bTB history going back 1, 2, 5 or more years? Each highlight the importance of bTB history on future risk. Each also suggests that the longevity of this risk is substantially longer than previously thought.

White et al. (2013) conducted a case–control study on the association between bTB restrictions in index herds in 2006 and in neighbouring herd(s) (within 1 km) in previous years, while controlling for each herd's bTB history and other risk factors. Past bTB history was found to be a significant risk factor for bTB recurrence, both of the neighbouring herds up to 2 years previously, and in the index herd up to 5 years previously. Indeed, after controlling for all other variables in the model, herds with a bTB restriction 5 years previously were 1.39 times more likely to suffer a bTB recurrence than herds without a bTB restriction during the last 5 years. In other words, bTB history was important, both in the index and neighbouring herds, with the effect persisting longer in the former.

Clegg et al. (2015b) considered the longevity of herd bTB risk in greater detail, to help refine existing policy and to support decision-making with respect to the enhancement of risk-based controls on herds following a restriction. Of the 111,214 'clear' herds with $\geq$1 full herd test during 2012, the study compared those that were (4479, 4.0%) and were not (106,735, 96.0%) restricted (with $\geq$1 standard reactor or visible lesion at slaughter). Consistent with previous studies, risk factors influencing the probability of a herd being restricted in 2012 included bTB history, herd size, number of adult animals purchased in the previous year, county incidence rate and the proportion of cows. Consistent with earlier studies, future risk increases with both increasing severity of, and decreasing time since, the previous restriction. Of particular importance, the study also suggests a future risk greater than baseline in those situations where the previous bTB restriction was both minor (a single standard reactor or lesion at slaughter) and many years previous. This suggests local persistence of infection (more likely in the locality rather than the herd) over relatively long time periods.

The introduction of cattle contributes to the establishment of bTB in Irish cattle herds. Herd bTB risk increases in association with an increase in the numbers of animals introduced (White et al., 2013). Further, the movement of animals in Ireland is substantial (Ashe et al., 2009), with animal-level bTB risk increasing with prior bTB exposure (Olea-Popelka et al., 2008; Wolfe et al., 2009). Nonetheless, the proportion of herd bTB restrictions attributable to introduction is relatively low, approximately 7%, based on analyses conducted on national data from April 2003 to March 2004 (Clegg et al., 2008) and during 2012 (Clegg et al., 2015b). These estimates were determined after evaluating the movement and related herd bTB history of all herds restricted in Ireland during these two 12-month periods. The estimates were underpinned by several assumptions. Firstly, exposure was used as a proxy for infection. Secondly, the studies focused solely on recently introduced animals, ignoring the potential for latency (animals becoming infected following exposure but passing at least one test following introduction). Departure from these two assumptions will result in opposing effects on the estimate (departure from the former will over-estimate risk, and from the latter, the converse) (Clegg et al., 2008).

Lane et al. (unpublished) assessed animal movements during 2011 to 2013, focusing on the 402,365 animals that moved into herds that subsequently had a bTB breakdown. Only 0.44% of the animals tested within two months of moving into such herds were skin test positive at that test. At this test, the animal-level bTB risk increased with duration of residence in, and the herd-level bTB risk associated with, the destination herd. As with Clegg et al. (2008), this suggests that bTB risk is dominantly associated with the herd rather than the moving animal. Further analysis is ongoing into herds from which the test positive animals originated, seeking to predict the bTB risk associated with individual animals prior to their outward movement.

3.2. Reasons for bTB persistence

3.2.1. General comments

In general terms, the problem of bTB persistence, either in a herd (herd recurrence) or a locality (local persistence), can be attributed to residual infection in cattle and/or re-infection, either from local sources (such as spread from environment, wildlife or farm-to-farm) or following cattle introduction. In recent years, there has been considerable research in Ireland on this issue, and substantial gains in understanding have been made. However, it has not generally been possible to be conclusive about either the role or relative importance of each of these different infection sources due, in part, to the broad-ranging control measures employed following high-risk breakdowns, which focus on both the herd and the locality. In such situations, it is often difficult to disentangle the relative importance of each infection source.

In Ireland, bTB-infected herds cluster in space, as outlined previously. Kelly and More (2011) found that spatial clustering persisted throughout a 5-year period of proactive badger removal (in the removal areas of the four area project). Badger numbers were substantially reduced, and this effect can be attributed to environmental contamination, residual (persistent but undetected) infection in cattle, and ongoing herd-to-herd transmission.

Good et al. (2011) evaluated the impact of full herd depopulation during 2003–2005 on bTB recurrence, by

comparing the future history of herds depopulated as a result of either bTB or BSE. In Ireland, the bTB depopulation policy is broad-ranging, focusing on all known drivers for bTB recurrence, including infected cattle, environmental contamination and, since 2000, a wildlife reservoir. Therefore, additional measures were employed during bTB (but not BSE) depopulation. Contrary to earlier depopulation studies in Ireland (Hahesy et al., 1992, 1996), the study found no significant difference in future bTB history, when comparing herds depopulated for bTB (by definition, those of high bTB risk) and BSE (those with no or a low previous bTB risk). Therefore, bTB depopulation during this period was effective in significantly reducing bTB risk, both in the herd (as a result of depopulation of infected cattle) and the locality (as a result of disinfection, delayed restocking to limit environmental contamination, contiguous testing and local badger removal).

Clegg et al. (2008) investigated the future bTB risk of 390,365 animals following derestriction of all Irish herds ($n = 3947$) during the 12 months from 1 October 2001. These herds had all previously been restricted following the detection of $\geq$2 standard reactors or bTB-lesioned animals. In total, 55,410 (14.2%) animals subsequently moved to new herds during the period between derestriction and the next full herd test, whereas 334,955 (85.8%) did not. The source herds were more likely than the destination herds to be located in areas where infection prevalence had been high for some years. Further, individual animal risk increased with increasing residence time in a herd following derestriction. Infection risk was significantly greater among non-movers (0.47%, 95% CI = 0.45–0.49%) compared to movers (0.22%, 0.18–0.26%). Further, among non-movers, infection risk increased with increasing time since derestriction. Infection risk was greater in the source (compared to the destination) herds, either as a result of cattle-to-cattle transmission (in this case, from residually infected cattle in the source herd or on neighbouring farms) or transmission from the environment, wildlife or humans. Again, the relative importance of each cannot be determined from this study.

3.2.2. The importance of residual infection in bTB persistence

3.2.2.1. General. A number of studies are providing insights into the importance of residual infection (that is infected, but undetected, cattle) in the epidemiology of bTB in Ireland. Berrian et al. (2012) conducted a retrospective cohort study to determine the bTB risk among animals moved from unrestricted herds during 2005. Comparison was made between animals moved from herds that had been restricted at some stage during 2005 ('exposed') compared with those that had not ('non-exposed'). The overall risk of a bTB diagnosis during the 2-year period after the animals were moved was 0.69%, with animals from 'exposed' herds being 1.91 (1.76–2.07) times more likely to test positive compared with animals from 'non-exposed' herds. The impact of control measures during a bTB restriction was substantial, with animals moved before the herd restriction date having a significantly higher risk of being classified as bTB positive compared with animals moved subsequently.

Similar results were obtained by Wolfe et al. (2009), who investigated the future bTB risk in cattle sold from dairy herds with a recent bTB history. In this study, comparison was made between animals from exposed herds (those experiencing a recent bTB restriction) and unexposed herds (those that did not). A number of risk factors were identified, including cow–herd size, and an interaction between age and sex. In addition, there was a trend of increasing risk with increasing exposure, for cattle moved within 7 months of herd derestriction following a bTB episode. In comparison with unexposed herds, animals from herds with 1–7 reactors were 1.23 (0.87–1.74) times more likely to test positive, and animals with 8 or more reactors were 1.77 (1.06–2.96) times more likely to test positive. This study provides evidence in support of persistent infection following large breakdowns of 8 or more total reactors. It was postulated that large breakdowns are associated with active within-herd transmission, both preceding and during herd restriction (Wolfe et al., 2009).

In Ireland, as elsewhere, bTB breakdowns are first detected through either field or abattoir surveillance. The latter is particularly important in Ireland: up to 36% of bTB breakdowns between 1995 and 2010 were first detected using this method (Abernethy et al., 2013). In approximately 80% of these breakdowns, no further reactors are detected at a full herd retest (the factory lesion test, FLT) (Olea-Popelka et al., 2008). In a detailed study comparing breakdowns where further reactors were and were not identified at the FLT, risk factors for additional reactors were each broadly linked with past bTB exposure. The risk factors varied depending on whether the index animal (the animal with gross lesions during abattoir surveillance) was introduced or homebred. If the index animal had been introduced, increased risk was associated with both the index herd (the number of months that the index animal had been present in the herd, the herd size, the number of contiguous herds) and the index animal (whether the animal had been present in a bTB episode in a previous herd). If the index animal was homebred, risk increased with a range of herd-level factors (time since last test, herd size, number of contiguous herds) and decreased with animal age. If the animal had been in a previous bTB restriction, risk increased with increasing time since this restriction. These results highlight the risk associated with a previous bTB episode, with this risk increasing with time and, reasonably, the opportunity for transmission of infection to cohort animals. If the animal had not been in a previous bTB episode, risk decreased with time that the index herd was clear of bTB.

3.2.2.2. Inconclusive reactors. Clegg et al. (2011b,c) recently evaluated the short- and long-term bTB risks of standard inconclusive reactors (SIRs, animals with a bovine response >2 mm and between 1 and 4 mm greater than the avian response) to the SICTT. The study was conducted on SIRs in otherwise bTB-free herds, thereby avoiding potential confounding factors caused by variations in test interpretation (as would occur if reactor animals were detected concurrently). SIRs (and TIRs; 'transient SIRs', these being SIR animals with a negative SICTT result at the

subsequent inconclusive reactor retest) had a higher risk of being declared bTB positive, compared to SICTT −ve cohort animals from the same herd, at each of four different periods of interest, as follows:

- *At slaughter, following an inconclusive response:* SIR animals were more likely to be slaughtered (reflecting an increased perception of risk among farmers) and positive at post-mortem (Clegg et al., 2011c).
- *At the inconclusive reactor retest:* at this test, the bTB reactor incidence among SIR animals was almost three times that of the national rate (Clegg et al., 2011c).
- Following a negative inconclusive retest result.
  - *Following movement to another herd:* 3.44% of the SIR animals that moved from the herd within 6 months of a clear retest were positive at the next test/slaughter, compared to 0.26% of the SICTT −ve cohort animals (Clegg et al., 2011c).
  - *If remaining in the same herd:* for TIRs that remained in the herd of disclosure, the time to diagnosis with bTB for TIRs was on average 78% shorter than for non-TIR animals (Clegg et al., 2011b).

At most of these testing opportunities, the past history of the animal could not have influenced interpretation of the test result.

In broad terms, a S/TIR could be either a non-infected animal returning a suspect result, often following exposure to environmental or other mycobacteria, or a bTB infected animal returning a suspect, rather than a positive, SICTT result, due to a broad range of factors that relate to the animal, such as co-infection with or exposure to other mycobacteria, the tuberculin and/or the method of administration (de la Rua-Domenech et al., 2006). The results from this study clearly highlight the presence of the latter, with S/TIRs having a higher risk of being declared bTB positive at each future testing opportunity, compared to SICTT −ve cohort animals from the same herds. Consequently, differential treatment of S/TIR animals is justified.

3.2.3. The importance of wildlife in bTB persistence

There has been an increasing understanding about the role played by badgers in the epidemiology of bTB in cattle in Ireland (Corner, 2006). There is little doubt that badgers are a maintenance host with spillback to cattle—essentially, an upstream driver of infection (More, 2009). Substantial supporting evidence is now available.

Infection with *Mycobacterium bovis* is endemic in Irish badgers (Murphy et al., 2010, 2011); however, prevalence is not uniform throughout the country (Furphy et al., 2012). There appears to be no geographic clustering of strain types associated with prevalence (Furphy et al., 2012). In areas where cattle are at high bTB risk, *M. bovis* prevalence in badgers is high: 36.3% using enhanced post mortem examination and bacteriological culture (but only 12.1% based on confirmed gross visible lesion detection alone) (Murphy et al., 2010). In areas where bTB prevalence in cattle is very low or absent, infection is still present in badgers, albeit at lower levels. Based on a recent 'greenfield' study, *M. bovis* infection was identified in 14.9% of the badgers using equivalent enhanced methods (but with a higher concentration of decontaminant) in areas of Ireland with historic low bTB herd prevalence, and very little opportunity over many years for cattle to badger transmission (Murphy et al., 2011). Corner et al. (2011) suggest that badger social structures and the longevity of infected animals make them an ideal maintenance host for *M. bovis* infection.

Results from two large field trials (the east Offaly trial, Eves, 1999; Ó Máirtín et al., 1998a,b; the four area trial, Griffin et al., 2005) provide consistent and conclusive evidence of spillover of infection from badgers to cattle. A significant fall in bTB prevalence in cattle was observed in both trials in areas where badgers were proactively removed, in comparison to control areas. Further, these differences have been sustained for prolonged periods subsequently, in the removal areas of both the east Offaly (Kelly et al., 2008) and four area (Byrne et al., 2014) projects. Relative to reactive culling, proactive badger culling in the east Offaly area was associated with a decrease in herd bTB incidence during the periods of both intensive (1989–1995) and less-intensive (1996–2004) badger removal. By 2004, significant decreases of 22% and 37% were observed in the entire and the inner proactive removal areas, respectively, with the size of this decrease increasing with time (Kelly et al., 2008). During 2007–2012 (5–10 years after the end of the four area project), herds within the former removal area had 0.53 the odds of a herd bTB restriction in any given year than a herd within the former reference area (Byrne et al., 2014).

Since 2004, Ireland has implemented a national programme of badger culling, specifically to reduce badger density in areas with chronic problems of bTB in cattle herds (Sheridan, 2011; Byrne et al., 2013). It seeks to facilitate the business of farming in tandem with the conservation of a healthy national badger population (Sheridan, 2011). This strategy, which forms part of national bTB eradication programme, draws on the experience of the east Offaly and four area projects (but noting that these trials did not explicitly evaluate different culling methods), and on key principles of infectious disease epidemiology, including control. Culling is initially conducted reactively (in response to cattle bTB breakdowns) then continued proactively, covering areas up to 2 km beyond the farm boundary (Byrne et al., 2013), leading to a significant reduction in badger density (Byrne et al., 2013) and changes to the spatial organisation and activity of badgers (O'Corry-Crowe et al., 1996). In contrast to the experience elsewhere (More et al., 2007), adverse effects on infection prevalence following focused badger removal have not been observed in Ireland, either in cattle (Griffin et al., 2005; Kelly et al., 2008; Olea-Popelka et al., 2009) or badgers (Corner et al., 2008a). During the four area project, there was an overall long term decrease in the prevalence of bTB in the re-emergent badger population in proactively culled areas, and no consistent trend in reactively culled areas (Corner et al., 2008a). Subsequently, there has been a substantial fall in bTB prevalence in badgers captured as part of the national programme during 2009–2012 (Byrne et al., unpublished).

Olea-Popelka et al. (2009) investigated the impact of targeted badger removal on the survival time to future bTB episodes in herds in and around areas where badgers were removed in county Laois, during 1989–2004. The authors conducted a survival analysis, with the main exposure in this study being the geographical location of herds relative to the area in which targeted badger removal was conducted, that is:

- Group 0: Reference (unexposed) herds, more than 500 m from an index herd (or any associated parcels) at the time of a bTB breakdown.
- Group 1: Index herds.
- Group 2: Herds <25 m from an index herd or any associated parcels (immediate neighbours).
- Group 3: Herds 25 < 150 m distant.
- Group 4: Herds 150 < 500 m distant.

Herds in areas around targeted badger removal (groups 2–4) had significantly longer survival times to future bTB episodes compared with herds outside these areas (group 0). Further, the future bTb risk in index herds (group 1) was no different to those in reference herds (group 0). Because group 1 herds are traditionally at greater risk of a future herd breakdown (for example, Olea-Popelka et al., 2004), these results suggest a beneficial impact of targeted removal on their survival time. Several aspects of the study design may lead to bias (more effective bTB control in cattle herds in Co. Laois compared with other counties, erroneous inclusion of some index herds where badger removal had not taken place, insufficient control of herd fragmentation), however, in each case, the effect will be towards the null. Overall, the study suggests that targeted badger removal had a beneficial effect on the survival time to future bTB episodes in herds in and around areas where badgers were removed.

Efforts towards development of a bTB vaccine for badgers using BCG (Bacillus Calmette-Guérin) have been described in detail elsewhere (Sheridan, 2011; Robinson et al., 2012). Briefly, a range of pen-based experiments have highlighted a protective effect in badgers to artificial bTB challenge using both the subcutaneous and mucosal routes of administration (Corner et al., 2007, 2008b,c; Lesellier et al., 2009). Issues relating to licensing (Murphy et al., 2008) and delivery (Kelly et al., 2011) have also been considered. A field trial was subsequently conducted over three zones covering approximately 755 km^2 in Co. Kilkenny (Corner et al., 2009; Aznar et al., 2011), and analyses are now underway, focusing on incidence (Aznar et al., 2013; Aznar et al., 2014) and prevalence data. A non-inferiority trial, comparing badger vaccination and culling, is currently being conducted in 6 counties in Ireland (J. O'Keeffe, pers. comm.).

3.2.4. The importance of cattle introductions in bTB persistence

In contrast to bTB establishment, it is unlikely that introduced animals are contributing to the observed pattern of bTB persistence in Ireland (that is, a bias towards herds with a previous history of bTB infection, thereby leading to infection that is clustered in both space and time). This would only be possible if the movement of infected animals were substantially biased towards herds with a known bTB history. Rather, it would be expected that introduced infection would lead to a relatively dispersed spatial pattern of infection (Kelly and More, 2011).

3.3. Local persistence: disentangling relative importance

White et al. (2013) describe the first work in Ireland to disentangle the various infection sources, and determine their relative importance. In this work, the authors specifically focus on the relative importance of 'neighbourhood', specifically farm-to-farm spread and spread from wildlife, in bTB persistence. A case-control study was conducted of Irish herds that did (the index herds) and did not experience a bTB episode during 2006. A multivariable model was developed incorporating a broad range of independent variables, related to both the index herd (herd history, herd size, number of animals purchased) and to neighbouring herds (zone 1: herds within 25 m; zone 2: herds between 26 and 150 m; zone 3: herds between 151 and 1000 m). In the study population, ~43% of bTB episodes in 2006 could be attributed to the bTB history in the index and neighbouring herds during the previous 2 years. The population attributable fraction of various infection sources were as follows:

- 15% to the bTB history of the index herd during 2001–2005;
- 20% to the bTB history of neighbouring herds that were directly contiguous (≤25 m) during 2004–2005; and
- 19% to the bTB history of neighbouring herds that were not directly contiguous (>25 m) during 2005.

Logically, contiguous spread will be limited to directly contiguous herds, whereas wildlife spread is not limited by contiguity. On this basis, the authors attribute 15% of the bTB episodes in the study to residual infection, between 0% and 20% to contiguous spread, and between 19% and 39% to wildlife. The relative value of these results is of particular interest, noting that other factors (some modeled: herd size, animals purchased; some currently not accounted for in the model) also contribute to future bTB risk. As noted by White et al. (2013), it would be useful to repeat these analyses in areas of the country where badger-to-cattle transmission is likely to have been minimised, such as within the areas of the four area project (Griffin et al., 2005) subjected to proactive badger removal. This would allow a better estimate of true cattle-to-cattle (herd-to-herd) spread among herds directly contiguous to one-another.

4. Managing bTB risk

Detailed information about the Irish bTB eradication programme has been presented previously, including policy changes, programme supports including data management systems, the wildlife disease control strategy, the use of diagnostics and quality control (More and Good, 2006; Sheridan, 2011; Duignan et al., 2012). The

national programme handbook is available online (Good et al., 2010).

In recent years, there have been three primary drivers for policy change: scientific advances, ongoing improvements to programme supports, and ongoing programme review. We will consider only the first two here. Following the work of Clegg et al. (2011b,c), policy changes were introduced in 2012 to confine inconclusive reactors to the herd of origin with a life-long movement restriction, except direct to slaughter. Drawing on the work of White et al. (2013), increased controls (testing, restrictions) have been placed on herds contiguous to high-risk bTB breakdowns. Ongoing technical improvements are also facilitating programme management. The national Animal Health Computer System (AHCS, a bespoke web-based management system for the Irish bTB eradication programme, fully operational since early 2005) has been specifically programmed to manage all aspects of the bTB eradication programme, thereby ensuring compliance with EU and national legislation and consistent application across the country. AHCS is closely integrated with the Animal Identification and Movement (AIM) system, allowing consistent application of both herd- and animal-based controls.

5. Evaluating national progress

An objective assessment of the national bTB situation in Ireland has become increasingly important, to allow critical evaluation of progress towards control and eradication. A number of performance measurements are routinely available (including bTB herd incidence, reactor animals per thousand tests [APT] and number of reactors removed), each highlighting a steadily improving situation. These trends are mirrored in a recent time-series analysis of restriction rates to the annual surveillance test in low risk herds (Gallagher et al., unpublished). Greater detail is increasingly available about defined aspects of the programme, including activities relating to surveillance and to control. Concerns about the effectiveness of abattoir surveillance have been identified (Frankena et al., 2007), including substantial between-abattoir variation during 2003–2004 with respect to both submission risk (the number of animals submitted with lesions divided by the number of attested animals killed) and confirmation risk (the number of animals with laboratory confirmed lesions divided by the number of animals submitted with lesions). At this time, there was a 9-fold difference in submission risk between abattoirs submitted lesions from at least 10 animals (range 7–65 per 10,000, average 22 per 10,000). Collins (1997) suggests that variations in factory surveillance efficiency may be due to factory-related circumstances, for example, line speed and light intensity, and/or to factors related to the veterinary inspector, for example, their experience, interest, motivation and workload. In a later study, using equivalent data from 2005 to 2007, improvement was evident, including an observed 5-fold difference in submission risk between abattoirs (range 11–58 per 10,000, average 25 per 10,000; Olea-Popelka et al., 2012). Between 2006 and 2012, the submission risk rose from 26.8 to 37 per 10,000, whereas the confirmation risk fell from 18.2 to 14.9 per 10,000. Clegg et al. (2015a) found evidence of improvement in testing effectiveness among private veterinary practitioners in 2011 compared with 2008 in a range of indices, which is likely attributable to programme quality control (Duignan et al., 2012). Herd recurrence remains problematic, with approximately 12% positive at the post-derestriction test (Abernethy et al., 2013). Nonetheless, there has been clear evidence of improvement, with 2008-derestricted herds being 0.74 times (95% confidence interval: 0.68–0.81) as likely to be restricted in the 3 years following derestriction compared with 1998-derestricted herds (Gallagher et al., 2013). McGrath et al. (2014) highlighted spatial changes in annual animal-level bTB incidence during 2008–2012 in comparison with the mean annual bTB incidence during 1998–2007, highlighting general improvement in latter periods.

6. Future challenges

6.1. How much additional effort is needed?

During the last 15 or so years, epidemiological research in Ireland has primarily focused on an improved understanding of bTB risk. This information has progressively been translated into substantial policy changes leading to measurable improvement in both surveillance (detecting infection in herds and animals) and control (clearing infection from herds, once detected). bTB is now under good control (Abernethy et al., 2013; Gallagher et al., 2013). It is clear, however, that final eradication will not be achievable with existing surveillance and control tools. In particular, we are not yet able to adequately limit ongoing infection from badgers, an upstream driver of infection in Ireland. In response, current research is primarily focused on two key areas: the potential of additional measures to further limit cattle-to-cattle transmission, and sustainable methods to limit badger-to-cattle transmission, in particular a bTB vaccine for badgers. Progress with the former will lead to a further drop in herd bTB incidence in Ireland, but not to the point of eradication. Critical information about the latter will become available shortly, based on results from the Kilkenny badger vaccination field trial (Sheridan, 2011; Aznar et al., 2011, 2013, 2014). A non-inferiority trial is currently being conducted in six counties in Ireland evaluating the relative impacts of badger culling and vaccination on herd-level bTB prevalence (J. O'Keeffe, pers. comm.).

The next logical question to be asked concerns the additional effort that will be required, to move towards final eradication. In terms of efforts to limit badger-to-cattle transmission, some key questions include: will ongoing culling be required? How effective does badger vaccine need to be, in terms of efficacy (efficacy for infectiousness, efficacy for susceptibility)? What level of vaccine coverage will be needed? Will ongoing culling be required? In terms of efforts to limit cattle-to-cattle transmission, we need to know what, if any, additional controls will be required, over and above those already in place? These issues are currently being explored, based on

calculations of the reproduction ratio of both the overall system and of its component parts (badger-to-badger, cattle-to-cattle, and interactions), given the current situation and under a range of control scenarios (I. Aznar, pers. comm.).

6.2. False positive reactors

A percentage of non-infected animals are falsely positive to current testing methods. This is an ongoing challenge, given the imperfect specificity of test methods (including the single intradermal comparative tuberculin test (SICTT) and interferon-γ assay), but will become more so, as the positive predictive value falls with reducing bTB prevalence.

The specificity of the SICTT has been estimated to be 99.5% (median, ranging from 78.8% to 100%) based on international studies in cattle populations free of bTB (de la Rua-Domenech et al., 2006), and 99.2–99.8% using latent class analysis on Irish samples without a gold standard (Clegg et al., 2011a). Non-specific reactors can occur following exposure to non-pathogenic environmental mycobacterial species (Gormley et al., 2013), including *M. hiberniae* (Cooney et al., 1997). The interferon-γ assay, with lower specificity, is primarily used in conjunction with the SICTT in severely infected herds or in groups of animals where the reduced specificity is considered acceptable (Gormley et al., 2006, 2013). Estimates of the specificity of the assay include 88.1–96.6% (depending on the cut-off used, Monaghan et al., 1997), 96.6% (median, de la Rua-Domenech et al., 2006), and 86.8–89.4% (Clegg et al., 2011a).

Ireland has operated a 'Singleton Protocol' since 1996, allowing the early restoration of disease-free status to herds with a single reactor, where bTB is not confirmed by epidemiological investigation, by postmortem examination or by further test (Good et al., 2010). Murray et al. (2012) evaluated the ability of the Protocol to identify false positive reactors, by comparing the animal lesion rate at slaughter and reactor retest breakdown rate in single reactor breakdowns, including those that were and were not eligible under this protocol. Significant differences were observed in animal lesion rate but not reactor retest breakdown rate, highlighting the value of the protocol, but also the potential for improvement in the classification used. Wolfe et al. (2010) has previously highlighted difficulties in the development of predictive statistical models for recurrence.

An improved understanding of risk factors for false positive results will assist with local decision-making. Gormley et al. (2013) used cohorts of animals from low prevalence tuberculosis herds to assess a range of risk factors that might influence the specificity of the interferon-γ assay. Risk factors for false positive results include animal age (with risk increasing with age) and region of herd origin. Of note, a high proportion of herds with multiple interferon-γ assay positive animals were located in one county, with evidence of within-herd clustering, suggesting a localised source of non-specific sensitization (Gormley et al., 2013). Forthcoming work is anticipated on the impact of proximity to peat land on SICTT performance, and on animals with SICTT responses at an otherwise clear herd test. Collectively, this information may assist in allowing test performance to be optimised, in order to reduce the disclosure rate of false positive reactors (Gormley et al., 2013). There has also been ongoing work to investigate the changing characteristics of bTb episodes (J. O'Keeffe, pers. comm.), providing further insights into the relative importance of false positive reactors in the Irish programme.

6.3. Re-engagement with the farming community

During 1988–1992, a new executive agency, ERAD, was created, with the task to provide more dynamic management of the programme and to reduce disease levels by half within a four-year time frame. Stakeholder ownership was important during this period, but has become much less prominent subsequently. Although there is a good case for government involvement (badgers as a protected species, the benefit from collective action in the eradication of this infectious disease, Devitt et al., 2013), industry is the main beneficiary of bTB control in Ireland. However, all aspects of programme governance are currently directed and delivered by government, and the contribution of industry to key aspects of governance, including policy formulation and programme management, is minimal (More, 2009). As highlighted by Sheridan (2011), a programme re-launch will be needed, once all critical constraints to eradication have been addressed. From this time, it will be important that stakeholders once again play a much greater role in programme ownership.

7. Conclusions

In conclusion, there is close interaction between science and policy in Ireland, seeking both to understand and effectively manage bTB risk. Substantial national progress is being made, and herd- and animal-level prevalence is falling. There has been substantial recent progress in the development of strategies to adequately limit ongoing infection from wildlife; if successful, it may soon to possible to address the remaining constraints to eradication. Substantial challenges remain, but there is a sound basis for considerable optimism.

Acknowledgements

We acknowledge the many people who have contributed to bTB research and policy in Ireland. In Ireland, bTB research is predominantly funded by the national Department of Agriculture, Food and the Marine.

References

Abernethy, D.A., Upton, P., Higgins, I.M., McGrath, G., Goodchild, A.V., Rolfe, S.J., Broughan, J.M., Downs, S.H., Clifton-Hadley, R., Menzies, F.D., la Rua-Domenech, de, R., Blissitt, M.J., Duignan, A., More, S.J., 2013. Bovine tuberculosis trends in the UK and the Republic of Ireland, 1995–2010. Vet. Rec. 172, 312-312.

Ashe, S., More, S.J., O'Keeffe, J., White, P., McGrath, G., Aznar, I., 2009. Survival and dispersal of a defined cohort of Irish cattle. Ir. Vet. J. 62, 44–49.

Aznar, I., Frankena, K., More, S.J., Whelan, C., Martin, W., Gormley, E., Corner, L.A.L., Murphy, D., De Jong, M.C.M., 2014. Optimising and evaluating the characteristics of a multiple antigen ELISA for detection of *Mycobacterium bovis* infection in a badger vaccine field trial. PLoS ONE 9, e100139.

Aznar, I., McGrath, G., Murphy, D., Corner, L.A.L., Gormley, E., Frankena, K., More, S.J., Martin, W., O'Keeffe, J., De Jong, M.C.M., 2011. Trial design to estimate the effect of vaccination on tuberculosis incidence in badgers. Vet. Microbiol. 151, 104–111.

Aznar, I., More, S.J., Frankena, K., De Jong, M.C.M., 2013. Estimating the power of a *Mycobacterium bovis* vaccine trial in Irish badgers. Prev. Vet. Med. 111, 297–303.

Berrian, A.M., O'Keeffe, J., White, P., Norris, J., Litt, J., More, S.J., Olea-Popelka, F.J., 2012. Risk of bovine tuberculosis for cattle sold out from herds during 2005 in Ireland. Vet. Rec. 170, 620-620.

Byrne, A.W., O'Keeffe, J., Sleeman, D.P., Davenport, J., Martin, S.W., 2013. Impact of culling on relative abundance of the European badger (*Meles meles*) in Ireland. Eur. J. Wildl. Res. 59, 25–37.

Byrne, A.W., White, P., McGrath, G., O'Keeffe, J., Martin, W., 2014. Risk of tuberculosis cattle herd breakdowns in Ireland: effects of badger culling effort, density and historic large-scale interventions. Vet. Res. 45, 109.

Clegg, T.A., Blake, M., Healy, R., Good, M., Higgins, I.M., More, S.J., 2013. The impact of animal introductions during herd restrictions on future herd-level bovine tuberculosis risk. Prev. Vet. Med. 109, 246–257.

Clegg, T.A., Duignan, A., Whelan, C., Gormley, E., Good, M., Clarke, J., Toft, N., More, S.J., 2011. Using latent class analysis to estimate the test characteristics of the γ-interferon test, the single intradermal comparative tuberculin test and a multiplex immunoassay under Irish conditions. Vet. Microbiol. 151, 68–76.

Clegg, T.A., Good, M., Duignan, A., Doyle, R., Blake, M., More, S.J., 2011. Longer-term risk of *Mycobacterium bovis* in Irish cattle following an inconclusive diagnosis to the single intradermal comparative tuberculin test. Prev. Vet. Med. 100, 147–154.

Clegg, T.A., Good, M., Duignan, A., Doyle, R., More, S.J., 2011. Shorter-term risk of *Mycobacterium bovis* in Irish cattle following an inconclusive diagnosis to the single intradermal comparative tuberculin test. Prev. Vet. Med. 102, 255–264.

Clegg, T.A., Duignan, A., More, S.J., 2015a. The relative effectiveness of testers during field surveillance for bovine tuberculosis in unrestricted low-risk herds in Ireland. Prev. Vet. Med., http://dx.doi.org/10.1016/j.prevetmed.2015.02.005.

Clegg, T.A., Good, M., More, S.J., 2015b. Future risk of bovine tuberculosis recurrence among higher risk herds in Ireland. Prev. Vet. Med. 118, 71–79.

Clegg, T.A., More, S.J., Higgins, I.M., Good, M., Blake, M., Williams, D.H., 2008. Potential infection-control benefit for Ireland from pre-movement testing of cattle for tuberculosis. Prev. Vet. Med. 84, 94–111.

Collins, J.D., 1997. Meat plant surveillance and its role in the eradication of tuberculosis in cattle. In: Selected Papers 1996. Tuberculosis Investigation Unit, University College Dublin., Dublin, pp. 55–59.

Cooney, R., Kazda, J., Quinn, J., Cook, B., Muller, K., Monaghan, M., 1997. Environmental mycobacteria in Ireland as a source of non-specific sensitisation to tuberculins. Ir. Vet. J. 50, 370–373.

Corner, L.A.L., 2006. The role of wild animal populations in the epidemiology of tuberculosis in domestic animals: how to assess the risk. Vet. Microbiol. 112, 303–312.

Corner, L.A.L., Clegg, T.A., More, S.J., Williams, D.H., O'Boyle, I., Costello, E., Sleeman, D.P., Griffin, J.M., 2008. The effect of varying levels of population control on the prevalence of tuberculosis in badgers in Ireland. Res. Vet. Sci. 85, 238–249.

Corner, L.A.L., Costello, E., Lesellier, S., O'Meara, D., Gormley, E., 2008. Experimental tuberculosis in the European badger (*Meles meles*) after endobronchial inoculation with *Mycobacterium bovis*: II. Progression of infection. Res. Vet. Sci. 85, 481–490.

Corner, L.A.L., Costello, E., Lesellier, S., O'Meara, D., Gormley, E., 2008. Vaccination of European badgers (*Meles meles*) with BCG by the subcutaneous and mucosal routes induces protective immunity against endobronchial challenge with *Mycobacterium bovis*. Tuberculosis (Edinburgh) 88, 601–609.

Corner, L.A.L., Costello, E., Lesellier, S., O'Meara, D., Sleeman, D.P., Gormley, E., 2007. Experimental tuberculosis in the European badger (*Meles meles*) after endobronchial inoculation with *Mycobacterium bovis*: I. Pathology and bacteriology. Res. Vet. Sci. 83, 53–62.

Corner, L.A.L., Murphy, D., Costello, E., Gormley, E., 2009. Tuberculosis in European badgers (*Meles meles*) and the control of infection with bacille Calmette-Guérin vaccination. J. Wildl. Dis. 45, 1042–1047.

Corner, L.A.L., Murphy, D., Gormley, E., 2011. *Mycobacterium bovis* infection in the Eurasian badger (*Meles meles*): the disease, pathogenesis, epidemiology and control. J. Comp. Pathol. 144, 1–24.

de la Rua-Domenech, R., Goodchild, A.V., Vordermeier, M., Hewinson, R.G., Christiansen, K.H., Clifton-Hadley, R., 2006. *Ante mortem* diagnosis of tuberculosis in cattle: a review of the tuberculin tests, gamma-interferon assay and other ancillary diagnostic techniques. Res. Vet. Sci. 81, 190–210.

Devitt, C., McKenzie, K., More, S.J., Heanue, K., McCoy, F., 2013. Opportunities and constraints to improving milk quality in Ireland: enabling change through collective action. J. Dairy Sci. 96, 2661–2670.

Duignan, A., Good, M., More, S.J., 2012. A review of quality control in the national bovine tuberculosis control programme in Ireland. Rev. Sci. Tech. Off. Int. Epiz. 31, 845–860.

Eves, J.A., 1999. Impact of badger removal on bovine tuberculosis in east County Offaly. Ir. Vet. J. 52, 199–203.

Frankena, K., White, P., O'Keeffe, J., Costello, E., Martin, S.W., van Grevenhof, I., More, S.J., 2007. Quantification of the relative efficiency of factory surveillance in the disclosure of tuberculosis lesions in attested Irish cattle. Vet. Rec. 161, 679–684.

Furphy, C., Costello, E., Murphy, D., Corner, L.A.L., Gormley, E., 2012. DNA typing of *Mycobacterium bovis* isolates from badgers (*Meles meles*) culled from areas in Ireland with different levels of tuberculosis prevalence. Vet. Med. Int. 2012, 742478–742486.

Gallagher, M.J., Clegg, T.A., Higgins, I.M., Williams, D.H., More, S.J., 2013. Comparison of bovine tuberculosis recurrence in Irish herds between 1998 and 2008. Prev. Vet. Med. 111, 237–244.

Griffin, J.M., Martin, S.W., Thorburn, M.A., Eves, J.A., Hammond, R.F., 1996. A case–control study on the association of selected risk factors with the occurrence of bovine tuberculosis in the Republic of Ireland. Prev. Vet. Med. 27, 217–229.

Griffin, J.M., Williams, D.H., Kelly, G.E., Clegg, T.A., O'Boyle, I., Collins, J.D., More, S.J., 2005. The impact of badger removal on the control of tuberculosis in cattle herds in Ireland. Prev. Vet. Med. 67, 237–266.

Good, M., Clegg, T.A., Duignan, A., More, S.J., 2011. Impact of the national full herd depopulation policy on the recurrence of bovine tuberculosis in Irish herds, 2003 to 2005. Vet. Rec. 169, 581.

Good, M., Duignan, A., Maher, P., O'Keeffe, J., 2010. Veterinary Handbook for Herd Management in the Bovine TB Eradication Programme. Department of Agriculture, Fisheries and Food http://www.agriculture.gov.ie/media/migration/animalhealthwelfare/diseasecontrols/tuberculosistbandbrucellosis/diseaseeradicationpolicy/TBHandbook2010070710.pdf.

Gormley, E., Doyle, M., Duignan, A., Good, M., More, S.J., Clegg, T.A., 2013. Identification of risk factors associated with disclosure of false positive bovine tuberculosis reactors using the gamma-interferon (IFNγ) assay. Vet. Rec. 44, 117.

Gormley, E., Doyle, M.B., Fitzsimons, T., McGill, K., Collins, J.D., 2006. Diagnosis of *Mycobacterium bovis* infection in cattle by use of the gamma-interferon (Bovigam) assay. Vet. Microbiol. 112, 171–179.

Hahesy, T., Griffin, J.M., Dolan, L.A., 1992. Study of herds depopulated due to tuberculosis. In: Selected Papers 1990–1991. Published by the Tuberculosis Investigation Unit, University College Dublin, , pp. 18–20, ISBN-1-870089-88-X.

Hahesy, T., Griffin, J.M., Collins, J.D., 1996. The prevalence of tuberculosis in herds reconstituted following a depopulation. In: Selected Papers 1995. Published by the Tuberculosis Investigation Unit, University College Dublin, , pp. 12–17, ISBN-1-898473-83-8.

Kelly, G.E., Condon, J., More, S.J., Dolan, L., Higgins, I., Eves, J., 2008. A long-term observational study of the impact of badger removal on herd restrictions due to bovine TB in the Irish midlands during 1989–2004. Epidemiol. Infect. 136, 1362–1373.

Kelly, D.J., Corner, L.A.L., Gormley, E., Murphy, D., Costello, E., Aldwell, F.E., Marples, N.M., 2011. Evaluation of attractant flavours for use in oral vaccine baits for badgers (*Meles meles*). Eur. J. Wildl. Res. 57, 767–774.

Kelly, G.E., More, S.J., 2011. Spatial clustering of TB-infected cattle herds prior to and following proactive badger removal. Epidemiol. Infect. 139, 1220–1229.

Lesellier, S., Corner, L., Costello, E., Lyashchenko, K., Greenwald, R., Esfandiari, J., Singh, M., Hewinson, R.G., Chambers, M., Gormley, E., 2009. Immunological responses and protective immunity in BCG vaccinated badgers following endobronchial infection with *Mycobacterium bovis*. Vaccine 27, 402–409.

Martin, S.W., Shoukri, M., Thorburn, M.A., 1992. Evaluating the health status of herds based on tests applied to individuals. Prev. Vet. Med. 14, 33–43.

McGrath, G., Clegg, T.A., More, S.J., 2014. Recent spatial changes in bovine tuberculosis in the Republic of Ireland. Vet. Rec. 175, 45.

Monaghan, M., Quinn, P.J., Kelly, A.P., McGill, K., McMurray, C., O'Crowley, K., Bassett, H.F., Costello, E., Quigley, F.C., Rothel, J.S., Wood, P.R., Collins, J.D., 1997. A pilot trial to evaluate the γ-interferon assay for the detection of *Mycobacterium bovis* infected cattle under Irish conditions. Ir. Vet. J. 50, 229–232.

More, S.J., 2009. What is needed to eradicate bovine tuberculosis successfully: an Irish perspective. Vet. J. 180, 275–278.

More, S.J., Clegg, T.A., McGrath, G., Collins, J.D., Corner, L.A.L., Gormley, E., 2007. Does reactive badger culling lead to an increase in tuberculosis in cattle? Vet. Rec. 161, 208–209.

More, S.J., Good, M., 2006. The tuberculosis eradication programme in Ireland: a review of scientific and policy advances since 1988. Vet. Microbiol. 112, 239–251.

Murphy, D., Corner, L.A.L., Gormley, E., 2008. Adverse reactions to Mycobacterium bovis bacille Calmette-Guérin (BCG) vaccination against tuberculosis in humans, veterinary animals and wildlife species. Tuberculosis (Edinburgh) 88, 344–357.

Murphy, D., Gormley, E., Collins, D.M., McGrath, G., Sovsic, E., Costello, E., Corner, L.A.L., 2011. Tuberculosis in cattle herds are sentinels for *Mycobacterium bovis* infection in European badgers (*Meles meles*): The Irish Greenfield Study. Vet. Microbiol. 151, 120–125.

Murphy, D., Gormley, E., Costello, E., O'Meara, D., Corner, L.A.L., 2010. The prevalence and distribution of *Mycobacterium bovis* infection in European badgers (*Meles meles*) as determined by enhanced post mortem examination and bacteriological culture. Res. Vet. Sci. 88, 1–5.

Murray, D., Clegg, T.A., More, S.J., 2012. Evaluation of single reactor bovine tuberculosis breakdowns based on analysis of reactors slaughtered at an Irish export meat plant. Vet. Rec. 170, 516.

O'Corry-Crowe, G., Hammond, R.F., Eves, J.A., Hayden, T.J., 1996. The effect of reduction in badger density on the spatial organisation and activity of badgers *Meles meles* L. in relation to farms in central Ireland. Biol. Environ. 96B, 147–158.

Olea-Popelka, F., Costello, E., White, P.W., McGrath, G.E., Collins, J.D., O'Keeffe, J.J., Kelton, D.F., Berke, O., More, S.J., Martin, S.W., 2008. Risk factors for disclosure of additional tuberculous cattle in attested-clear herds that had one animal with a confirmed lesion of tuberculosis at slaughter during 2003 in Ireland. Prev. Vet. Med. 85, 81–91.

Olea-Popelka, F.J., Fitzgerald, P., White, P., McGrath, G., Collins, J.D., O'Keeffe, J., Kelton, D.F., Berke, O., More, S.J., Martin, S.W., 2009. Targeted badger removal and the subsequent risk of bovine tuberculosis in cattle herds in county Laois, Ireland. Prev. Vet. Med. 88, 178–184.

Olea-Popelka, F.J., Freeman, Z., White, P., Costello, E., O'Keeffe, J., Frankena, K., Martin, W., More, S.J., 2012. Relative effectiveness of Irish factories in the surveillance of slaughtered cattle for visible lesions of tuberculosis, 2005–2007. Ir. Vet. J. 65, 2.

Olea-Popelka, F., White, P.W., Collins, J.D., O'Keeffe, J.J., Kelton, D.F., Martin, S.W., 2004. Breakdown severity during a bovine tuberculosis episode as a predictor of future herd breakdowns in Ireland. Prev. Vet. Med. 63, 163–172.

Ó Máirtín, D., Williams, D.H., Dolan, L., Eves, J.A., Collins, J.D., 1998. The influence of selected herd factors and a badger-intervention tuberculosis-control programme on the risk of a herd-level trade restriction to a bovine population in Ireland. Prev. Vet. Med. 35, 79–90.

Ó Máirtín, D., Williams, D.H., Griffin, J.M., Dolan, L.A., Eves, J.A., 1998. The effect of a badger removal programme on the incidence of tuberculosis in an Irish cattle population. Prev. Vet. Med. 34, 47–56.

Robinson, P.A., Corner, L.A.L., Courcier, E.A., McNair, J., Artois, M., Menzies, F.D., Abernethy, D.A., 2012. BCG vaccination against tuberculosis in European badgers (*Meles meles*): a review. Comp. Immunol. Microbiol. Infect. Dis. 35, 277–287.

Sheridan, M., 2011. Progress in tuberculosis eradication in Ireland. Vet. Microbiol. 151, 160–169.

White, P., Martin, S.W., De Jong, M.C.M., O'Keeffe, J.J., More, S.J., Frankena, K., 2013. The importance of "neighbourhood" in the persistence of bovine tuberculosis in Irish cattle herds. Prev. Vet. Med. 110, 346–355.

Wolfe, D.M., Berke, O., More, S.J., Kelton, D.F., White, P.W., O'Keeffe, J.J., Martin, S.W., 2009. The risk of a positive test for bovine tuberculosis in cattle purchased from herds with and without a recent history of bovine tuberculosis in Ireland. Prev. Vet. Med. 92, 99–105.

Wolfe, D.M., Berke, O., Kelton, D.F., White, P., More, S.J., O'Keeffe, J., Martin, S.W., 2010. From explanation to prediction: a model for recurrent bovine tuberculosis in Irish cattle herds. Prev. Vet. Med. 94, 170–177.