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Assessing the variability in transmission of bovine tuberculosis within Spanish cattle herds

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ABSTRACT

In Spain, despite years of efforts to eradicate bovine tuberculosis (bTB), the disease is still endemic, with some areas of high prevalence. In this context, the surveillance and control plans may need to be re-evaluated, and understanding the dynamics of bTB spread within Spanish herds may help to develop new strategies for reducing the time for detection of infected herds and for the elimination of bTB from the herds already infected. Here, we developed a compartmental stochastic model to simulate bTB within-herd transmission, fed it with epidemiological data from 22 herds (obtained from a previous work) and carried out parameter inference using Approximate Bayesian Computing methods We also estimated the "Within-herd transmission potential Number" (R_h), i.e. the average number of secondary cases generated by a single animal infected introduced into a totally susceptible herd, considering different scenarios depending on the frequency of controls. The median global values obtained for the transmission parameters were: for the transmission coefficient (β), 0.014 newly infected animals per infectious individual per day (i.e. 5.2 per year), for the rate at which infected individuals become infectious (α), 0.01 per day (equivalent to a latent period of 97 days), and for the rate at which infected individuals become reactive to the skin test (α_1), 0.08 per day (equivalent to a period of 12 days for an infected animal to become reactive). However, the results also evidenced a great variability in the estimates of those parameters (in particular β and α) among the 22 herds. Considering a 6-month interval between tests, the mean R_h was 0.23, increasing to 0.82 with an interval of 1 year, and to 2.01 and 3.47 with testing intervals of 2 and 4 years, respectively.

1. Introduction

Bovine Tuberculosis (bTB) is defined as a chronic infectious disease of cattle (including all *Bos* species, and *Bubalus bubalis*) and bison (*Bison bison*) caused by any of the disease-causing mycobacterial species within the *Mycobacterium tuberculosis*-complex (Anon., 2013a). Cattle are mainly affected by *Mycobacterium bovis* and *Mycobacterium caprae*, which can also affect other domestic and wild animals as well as humans (Anon., 2013b; De la Rua-Domenech et al., 2006; Aranaz et al., 2003). Due to its zoonotic nature and the high economic impact on livestock production, the objective within EU countries is the elimination of bTB through the implementation of eradication programs (Reviriego Gordejo and Vermeersch, 2006).

In Spain, it was not until 1993 that most dairy and beef herds were included within the bTB national eradication program (Anon., 2010). According to the programme, all cattle herds are routinely screened by the single intradermal tuberculin test (SITT), testing all animals above 6 weeks of age. Private veterinarians, accredited to provide government

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services, are in charge of performing the tests, which are usually carried out annually, although the frequency may be increased depending on the prevalence in the area. Positive cattle (reactors) are slaughtered and subjected to *post-mortem* examination at the slaughterhouses. Positivity is confirmed by culture of the mycobacteria. Other measures include passive surveillance for bTB lesions at the slaughterhouses. Thanks to the application of the national eradication program in cattle, bTB herd prevalence in Spain decreased from 5.90% in 1993 to 1.80% by the end of 2004 (Anon., 2015a). Afterwards, the bTB prevalence remained quite stable for over one decade (1.72% in 2014), despite the implementation of further measures such as the introduction of compulsory pre-movement tests in 2006 or the establishment of a surveillance plan for wildlife reservoirs in 2009. In 2015 there was a major setback, as bTB prevalence increased to 2.81%, similar to the levels Spain had in 2001 (Anon., 2015b). Within the country the situation is also quite heterogeneous with some regions free of bTB (e.g. the Canary Islands) or with very low prevalence (mainly the north of Spain), and others with very high prevalence, mainly central and southern Spain (e.g. herd prevalence in Andalusia in 2015 was 17.2%) (Allepuz et al., 2011; García-Saenz et al., 2014; Anon., 2015b).

Those results demonstrate the need to re-evaluate the measures currently in place if eradication is to be achieved. Understanding the dynamics of bTB spread within Spanish herds would be helpful for the design of new surveillance and control strategies that would reduce the time needed for both the detection of infected herds and the elimination of the disease from the infected herds.

Dynamic modelling of bTB has been widely applied because studying bTB spread in infected herds is hindered by the long incubation periods; and therefore models offer the opportunity to assess bTB transmission in a more cost-effective way (Brooks-Pollock et al., 2014; Conlan et al., 2012; Pérez et al., 2002). Different mathematical models have been used to describe the dynamics of bTB infection in the herd, with the purpose of estimating bTB within-herd transmission rates and evaluating the effectiveness of surveillance and control strategies (Barlow et al., 1997; Pérez et al., 2002; Álvarez et al., 2012a; Bekara et al., 2014; Brooks-Pollock et al., 2014; O'Hare et al., 2014). As a result, the bTB transmission parameters estimated are quite variable, which may be partially explained by the intrinsic variability in the transmission process, but also on factors such as the modelling approach used, the assumptions made, or the type and quality of the data used to feed models. Transmission dynamics is also influenced by the herd production type or the management practices, and therefore it is essential that parameters are obtained using data from herds that are representative of the bTB context in Spain.

In the present work, we first estimated the variability in the parameters related to bTB transmission in Spanish herds. Then, we used those parameters to simulate the average number of secondary cases caused by a single infected animal introduced into a herd, calling this "quantity" the "Within-herd transmission potential Number" (R_h).

2. Materials and methods

2.1. Selection of herds for parameter inference

In Spain, when a newly infected herd is confirmed by bacteriological culture, a veterinary officer carries out an epidemiological questionnaire, and the data is recorded in a database called BRUTUB, which is maintained by the Spanish Ministry of Agriculture, Fisheries, Food and Environment (Anon., 2010). In a previous work, Guta et al. (2014) developed a methodology to determine the most likely source of infection of bTB affected herds. Briefly: seven possible origins of infection were considered: i) residual infection; ii) purchase of cattle; iii) sharing of pastures; iv) neighbours; v) contact with domestic goats; vi) interaction with wildlife reservoirs and vii) contact with humans. Decision trees were developed for each of the different sources of infection, and a group of bTB experts assigned the probabilities for the possible events on those decision trees. By feeding the data from a given farm (contained in the BRUTUB questionnaire) to the decision trees, the probabilities of the farm being infected by each of the seven possible sources were quantified.

For the inference of bTB transmission parameters, we selected only infected herds in which we had some certainty that the introduction of bTB into the herd had occurred through purchase of animals, by adapting the methodology developed by Guta et al. (2014). More specifically, from the herds recorded in the BRUTUB database between 2010 and 2013:

a) First, we selected herds that met the criteria in relation to introduction through purchase of animals, that is: i) cattle had been purchased between the last negative control and the detection of infection in the herd of destination; ii) at least one of the purchased animals reacted positive to the SITT at the time of detection; iii) the herd of origin of cattle was subsequently confirmed as bTB infected; iv) and the same spoligotype was isolated in both herds or the same spoligotype was isolated during the previous year in the municipality of the herd of origin of introduced cattle.
b) Then, from the herds selected, we excluded those that did not meet the criteria of exclusivity in relation to the introduction of bTB only through purchase of animals. It means we further excluded all herds in which the introduction of the disease through any of the other sources was possible. In order to do that, we defined some other "key events" as exclusion criteria. For example, herds with evidence of the presence of some reactor 3 years prior to the last negative control were excluded because of potential residual infection; and herds that reported some sort of contact with wildlife reservoir species were excluded because of potential infection from wildlife.

Besides, any herd with missing data that did not allow ruling out any of the possible origins was also excluded for parameter inference.

2.2. Herd data for parameter inference

On those selected herds, data available included:

a) Date of purchase of animals from the herd subsequently found to be infected, i.e. the likely date of introduction of bTB into the herd.
b) Date of bTB detection in the herd.

We assumed that the difference between both dates represented the time available for the spread of bTB.

- Number of animals in the herd on the date of bTB detection.

We assumed a constant population size between infection of the herd and detection.

- Number of positives on the date of bTB detection.
- Number of positives among the purchased animals. As it is estimated at the time of detection, not at the time of purchase, it actually represents the maximum number of infected animals introduced into the herd (i.e. the number of occult animals introduced is modelled as a *Uniform* distribution between 1 and the number of positives among the purchased animals).

The difference between the number of infected among the purchased animals and the total infected animals in the herd on the date of bTB detection represented the spread of the infection within the herd since the introduction of bTB.

2.3. Development of the bTB spread model

Bovine tuberculosis within-herd transmission was simulated using a