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Research paper

Simulating control of a focal wildlife outbreak of *Echinococcus multilocularis*

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ABSTRACT

The parasitic tapeworm *Echinococcus multilocularis* is the causative agent of alveolar echinococcosis, a serious zoonotic infection present in Europe that can be fatal. The United Kingdom currently has *E. multilocularis* free status but the possibility of introduction exists, most likely via an imported or returning dog or other deliberately introduced animal that has not had anthelmintic treatment. We have developed a model to predict the probability of successfully eliminating a focal outbreak of *E. multilocularis* using a programme of anthelmintic bait distribution. We investigated three different potential control programmes, each with 36 monthly campaigns commencing five, ten or 15 years after disease introduction over an area of 2827 km^2. We assumed equilibrium disease prevalence of 30%, 40% and 55% based on the range of values reported across Europe. However, for all of these scenarios, equilibrium had not been reached at five to 15 years after introduction and simulated local prevalence values were between 0.5% and 28%. We found that it is possible to eliminate the disease with a 38%–86% success rate if control is started five years after introduction, dropping to 0% to 56% if control is delayed until 15 years after introduction, depending upon the prevalence equilibrium. We have also estimated the costs involved in these programmes to be from €7 to €12 million (2013 prices).

1. Introduction

Echinococcus multilocularis is a taeniid tapeworm found in the Northern Hemisphere, including Europe, where the red fox (*Vulpes vulpes*) and various vole species are the most important definitive and intermediate hosts respectively. It is the causative agent of alveolar echinococcosis (AE), a serious zoonotic disease. Its range is expanding in mainland Europe (Combes et al., 2012; Davidson et al., 2012; Gottstein et al., 2015; Romig, 2002; Vervaeke et al., 2006a,b) which increases the probability of introduction into disease-free countries such as the United Kingdom (UK). Were the disease to become established in the UK, it would have serious implications for human health, but if detected early enough after introduction, there is a possibility of eliminating the outbreak using anthelmintic baits. We have therefore developed an individual based model to investigate the probability of successful elimination.

The most likely route of introduction into UK wildlife is via the import of an infected dog (EFSA AHAW Panel (EFSA Panel on Animal Health and Welfare), 2015). The UK has therefore adopted the EU Pet Travel Scheme (PETS), but with a derogation for a requirement for anthelmintic treatment for dogs entering the UK from the EU. There are additional requirements for pets entering from other countries (Defra, 2016). The European Food Safety Authority (EFSA) suggested that this derogation reduces the probability of introducing *E. multilocularis* via domestic pets to a negligible level (Gunn et al., 2004). Without these safeguards, an introduction may well be inevitable: Torgerson and Craig (2009) estimated that for every 10,000 dogs imported or returning from a high endemic part of Europe, the probability that one is infected is >98%. EFSA have published a model to predict the probability of introduction of an infected dog into a previously *E. multilocularis* free country and state that it is 'inevitable', but that it would not necessarily result in the disease becoming established (EFSA AHAW Panel (EFSA Panel on Animal Health and Welfare), 2015). The number of dogs recorded entering the UK under the PETS scheme had risen from 12,633 in 2000–93,719 in 2008, the last year for which statistics are readily available (Defra, 2009), and a figure of 164,836 has been quoted for 2015 (The Kennel Club, 2016). The number of commercial imports has also risen over this time (The Lawn Veterinary Centre, 2016). It is difficult to obtain figures on the number of illegal imports, but two leading UK animal charities believe that there has been an increase associated with the introduction of the PETS scheme

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(DogsTrust, 2015; RSPCA, 2016). There is concern that these illegal imports, principally from Eastern Europe, are a likely route to introduction (Forster, 2013). Despite their predicted role in disease introduction, we have not considered dogs as having a role in ongoing disease transmission and have not considered them as a host in this model. Prevalence rates in domestic dogs are high, up to 19% in parts of Asia (Craig et al., 2017 in press) but are generally less than 1% in Europe (Dyachenko et al., 2008) although they may be as high as 8% (Deplazes et al., 2011) and because of their higher density in urban areas, they may contribute up to 19% of eggs in the environment (Hegglin and Deplazes, 2013). However, a lack of robust quantitative estimates of many key parameters, including dog density and differences between Europe and the UK in both the structure of the urban/suburban environment and the culture of dog ownership, resulted in the decision to exclude them from the model. The practices of feeding of dogs in the UK and their exercise routines may result in lower consumption of voles than in Europe and less likelihood that they will defecate in areas accessible to voles so they may have less of a role in continuing the disease cycle.

While dogs may receive the most attention, there are other possible introduction pathways: there were 98 beavers imported into the UK between 2001 and 2010 (Defra, 2012). Many of these animals were imported for the purpose of reintroduction and were deliberately released into the wild. In addition, they are frequently reported to escape from their enclosures.

There are comprehensive regulations controlling the import of beavers into the UK but despite this, in 2010, a beaver was found to have been infected with *E. multilocularis* at post-mortem (Kosmider et al., 2013) This animal had been quarantined on arrival for six months in accordance with the regulations. A risk assessment published by DEFRA considered the risk of a beaver imported from an endemic area resulting in the establishment of the disease in wildlife the UK to be low but uncertain. (Defra, 2012). Low is defined as 'rare but does occur'.

E. multilocularis control programmes have been attempted across Europe and Asia (Antolova et al., 2006; Hegglin and Deplazes, 2008; Hegglin et al., 2003; Inoue et al., 2007; König et al., 2008; Schelling et al., 1997; Tsukada et al., 2002) all summarised in Hegglin and Deplazes (Hegglin and Deplazes, 2013), plus other studies (Comte et al., 2013; Hansen et al., 2003; Nonaka et al., 2006; Romig et al., 2007; Tackmann et al., 2001). A meta-analysis of control programmes was carried out as part of a review by EFSA (Casulli et al., 2015). All of these studies demonstrated that anthelmintic baits could successfully reduce the prevalence of *E. multilocularis* in the controlled area, but long term elimination was not achieved. All were within regions of long-standing endemicity, or at the edge of an advancing endemic front as in Slovakia (Antolova et al., 2006). It is likely, therefore, that reinvasion would have occurred from the surrounding untreated area or there may have been residual infection within the controlled area from untreated foxes, environmental contamination with *E. multilocularis* eggs or infected voles (Takumi and Van der Giessen, 2005). The disease was permanently cleared from the Japanese island of Rebun by the elimination of the introduced fox population (Minagawa, 1999) but in this case reinvasion was not possible and any residual infection would eventually have disappeared in the absence of the primary host. One control programme in Germany did report complete elimination by the end of the control period but only within the central part of a larger control area, and long term results were not reported (Schelling et al., 1997).

In Sweden, *E. multilocularis* was first discovered in a single fox by a routine surveillance programme in 2011 and an analysis by the authorities indicated that elimination was possible as it was believed that this case represented a focal outbreak originating from the import of an infected dog. However, the discovery over the next few months of infected foxes from other parts of the country showed that it was not a recent outbreak and the attempt at control was abandoned and surveillance was increased instead (Lind et al., 2011; Wahlström et al., 2015; Wahlström et al., 2012).

The UK (along with Malta) is fairly unique as it is an island with long term border controls for *E. multilocularis*. There have been no cases of infection in >2000 red foxes tested since 2005 (Learmount personal communication) and no autochthonous human cases, suggesting that the UK is disease free. As this surveillance is ongoing there is a strong possibility that if infection is found, it will be a focal outbreak as a result of a recent incursion and therefore a rigorous control programme has a potentially higher chance of success than the scenarios described above.

For a focal outbreak control programme, the time to discovery of the disease is critical because the spatial extent of the infected area must be small for the control programme to be logistically feasible. Infection in wildlife is unlikely to be detected through casual field observation as neither the definitive nor the intermediate host show any clinical signs of infection. Domestic dogs are also asymptomatic and are unlikely to receive a diagnostic examination during routine deworming. There are, therefore, two likely routes to discovery of the disease: the presentation of a case of human AE or via the UK's *E. multilocularis* disease surveillance programme (EFSA, 2014). Human AE can be asymptomatic for up to 15 years (Eckert, 2001), and it may be a number of years before the first person is infected. The first diagnosis of human AE in Rebun was within 12 years of the introduction of infected foxes there (Minagawa, 1999). Discovery by the UK's fox surveillance programme may be quicker. It is designed to detect a national prevalence of no more than 1% at a confidence level of at least 95% for which a sample size of 340 foxes per year is required. The probability of discovering a local outbreak has not yet been assessed, since spatial extent and prevalence will change with time. We therefore selected five, ten and 15 years after introduction for the start of control to investigate the likelihood of elimination over these time scales.

The effort and resources required to control *E. multilocularis* are considerable. It is important therefore that the exercise has a high degree of predicted success. Comte et al. (2013) and Hegglin and Deplazes (2013) present brief outlines of costs for two control exercises which varied between €60 and €114 (2013 costs) per campaign per km^2 for control and costs for surveillance that were €51 per survey per km^2. We investigated the efficacy of a programme with twelve baiting campaigns per year for three years over an area up to 3000 km^2, similar in area to a control programme carried out in south west Germany in 1995 (Romig et al., 2007). For the control programmes we investigated, total costs using the figures quoted above would be between €7 million and €12 million (2013 costs) excluding any management, publicity, analysis, etc.

There have been a number of attempts to model the epidemiology of *E. multilocularis*. Besides the eight reviewed in Atkinson et al. (2013) a further seven were identified (Hansen et al., 2004; Ishikawa, 2006; Kim and Ahn, 2015; König and Romig, 2010; Lewis et al., 2014; Liu et al., 2015; Milner-Gulland et al., 2004; Nishina et al., 2006; Otero-Abad et al., 2017; Takumi et al., 2012). Most of these models analysed equilibrium endemic conditions although two (Hansen et al., 2003; Takumi and Van der Giessen, 2005 Takumi and Van der Giessen, 2005) addressed post-control 'bounce-back' and one (Takumi et al., 2008) addressed rate of spatial spread into the Netherlands from the European endemic area, but assumed an initially localised focus of infection.

The aims of this study were: to simulate the spread of *E. multilocularis* across a representative rural UK landscape following a focal outbreak, to investigate the probability of eliminating the outbreak under different equilibrium prevalence conditions, to investigate the effect of time lag between outbreak and the initiation of control