



Bluetongue transmission and control in Europe: A systematic review of compartmental mathematical models

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ABSTRACT

The growing frequency of bluetongue virus (BTV) incursions in Europe in recent years led to the largest BTV outbreak ever recorded in 2006/09, with a dramatic impact on the cattle and sheep industries. The complex epidemiology of this vector-borne disease of ruminants and its recent emergence need to be better understood to identify and implement efficient control strategies. Mathematical models provide useful tools for that purpose; many of them have been developed in the light of the 2006/09 outbreak. We aimed to provide a systematic review of compartmental mathematical models dedicated to BTV occurrence or transmission in European countries, to assess robustness of findings to different modelling approaches and assumptions. We identified relevant papers from PubMed and Scopus databases, 21 of which were included in the review following the selection process laid out in the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement. We systematically extracted data from these papers to address the diversity and evolution of modelling approaches, and to identify important characteristics for future model development. Then, we summarized the main insights provided into bluetongue epidemiology, and discussed the relevance of these models as tools for risk mapping and for the design of surveillance and control systems. On the whole, the mechanistic models reviewed provided flexible frameworks, yielding mostly epidemiological insights specific to geographical areas and study periods. Despite the limitations of these models that sometimes relied on strong assumptions, we advocate their use to facilitate and inform evidence-based decision-making in animal health.

1. Introduction

Bluetongue (BT) is a vector-borne viral disease of domestic ruminants and wild ungulates resulting from infection by a double stranded RNA virus of the genus *Orbivirus*, the Bluetongue virus (BTV), having 27 known serotypes (Schulz et al., 2016; Zientara et al., 2014). Animal-to-animal transmission is mainly achieved by biting midges of the genus *Culicoides* but direct transmission (transplacental or sexual) has also been observed (De Clercq et al., 2008). Disease outcome varies depending on the serotype and species involved (Mellor and Boorman, 1995), ranging from the absence of clinical signs to mild fever, facial oedema and even death and abortion. BT is qualified as notifiable under European legislation (Directive 2007/75) and OIE rules (Terrestrial Animal Health Code). BT spread is mainly controlled by movement and trade restrictions around infected areas, and serotype specific vaccination campaigns. It is a disease of severe economic consequence, mostly because of the indirect losses resulting from the control measures implemented following its detection (Rushton and Lyons, 2015).

Before the 21st century, Europe faced sporadic incursions of BTV from Africa and the Middle-East. Suitable conditions for BT spread seemed to be fulfilled only in parts of Portugal, and Spain, in Cyprus and in some Greek islands (Mellor et al., 2008). From 1998, Europe has experienced a dramatic change in BT epidemiology with more frequent incursions, reaching countries that had never previously reported BT cases such as many Balkan states, France (Corsica) and Italy (Mellor et al., 2008; Saegerman et al., 2008). In 2006, Bluetongue virus serotype 8 (BTV-8) was detected in Europe for the first time in the Maastricht region of the Netherlands, causing a massive outbreak in Western and Central Europe, eventually controlled in 2009 (Carpenter et al., 2009). Simultaneously, BTV-1 was detected in Spain, Portugal and South-West France in 2007 (Wilson and Mellor, 2009), BTV-6 in the Netherlands and Germany in 2008, and BTV-11 in Belgium in 2009. BTV-4, detected in Sardinia in 2012, spread through Eastern Europe between 2014 and 2017, reaching 17 countries (Sailleau et al., 2018). BTV-8 was not detected in Europe from 2009 until 2015 when it re-emerged in central France in a still on-going outbreak.

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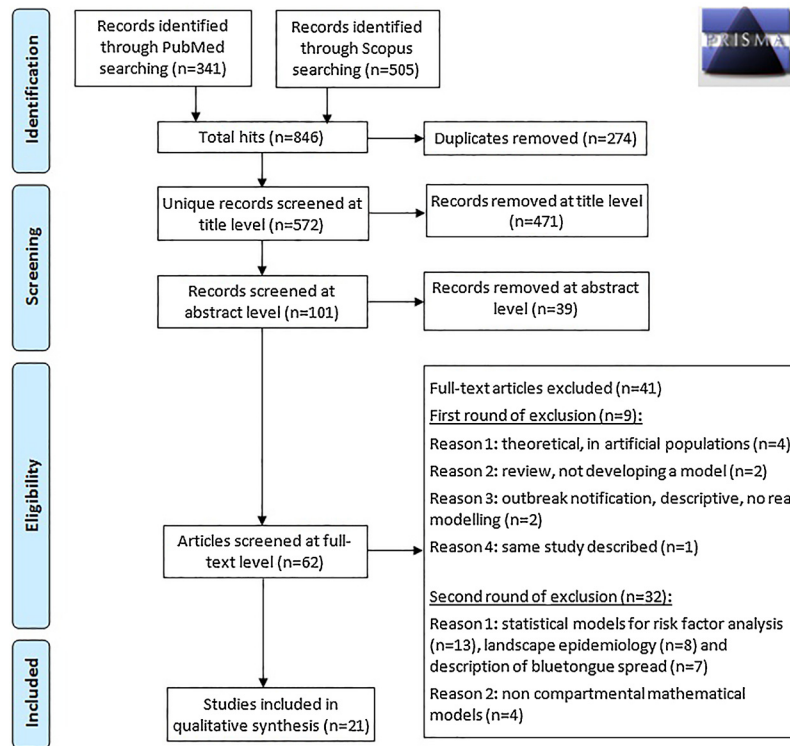


Fig. 1. PRISMA flow diagram representing the selection process.

In the past decades, many models have been developed to understand the significant changes in the complex BTV epidemiology in Europe and to assess the efficiency of surveillance programs and control measures. We can distinguish statistical modelling (including risk factor analysis and landscape epidemiology) from mathematical modelling: risk factor analysis refers to observational studies linking potential risk factors to real outbreak data; landscape epidemiology is a complementary approach, producing risk-maps from the geographic distribution of hosts, vectors and risk factors; whereas mathematical modelling provides explicit frameworks representing the dynamics of disease transmission by mathematical expressions. They can be used to compute various indicators of disease spread. A compartmental model is a mathematical model in which individuals are characterized by their state in a discrete state space, using systems of equations to describe the transitions between these states.

As the development of such models has increased in recent years, and given their potential importance in supporting evidence-based decision making in animal health, a review of the literature was considered of relevance. We therefore conducted a systematic review and analysis of the published studies of compartmental mathematical models of disease transmission, dedicated to the risk of BTV occurrence or transmission, and applied to European countries since 1998. We addressed the diversity of techniques developed to model BT transmission, identified the main insights provided into BT epidemiology, and discussed the relevance of these models as tools for risk mapping and for the design of surveillance and control systems.

2. Methods

2.1. Search terms and databases

This review follows the guidelines for systematic reviews and meta-analyses as laid out in the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement (Liberati et al., 2009). We focused on the specific case of BTV in Europe as the composition of vector populations diverges from the other continents. We

did not consider papers published prior to 1998, the year which marks the shift in BT epidemiology in Europe (Mellor et al., 2008; Saegerman et al., 2008). PubMed and Scopus databases were searched electronically from “1998-01-01” till “2017-07-14”, using the terms “bluetongue” or “*Culicoides*” and separately “model”, or “spatial”, or “risk factor”, using the “all fields” option to allow retrieval of articles in which the search terms appeared in the titles, abstracts, or keywords. All data were extracted and screened by the same researcher. Duplicates were removed and the selection of studies for inclusion was made in a multi-stage approach. Articles were first selected from the search results based on titles, excluding those deemed irrelevant to the topic. Their reference lists were scanned for additional literature. Articles were then selected based on abstracts to identify the final list of publications for full text reading, including those for which inclusion from abstracts was uncertain. These articles went through a full-text review and a second set of inclusion / exclusion criteria was applied to further refine the scope of the study.

2.2. Inclusion and exclusion criteria

In a first step, the following inclusion criteria were used: English written articles using statistical and mathematical modelling approaches to model BTV risk in animals; and the following exclusion criteria were applied: reviews, statistical analyses and models built in a non-European context, outbreak notifications and descriptions of epidemic situations (with no modelling), descriptions of clinical disease, pathogenicity and diagnosis, experimental infections in animals, development of vaccines, genome sequencing alone, entomological surveys alone, purely theoretical papers not yielding any practical guidance. Then, a second step of selection was performed among the statistical models for BTV spread to include only mathematical compartmental models. The additional exclusion criteria were: statistical models for risk factor analysis, landscape epidemiology, non-mathematical description of BT spread and non-compartmental mathematical models.

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