Detection, forecasting and control of infectious disease epidemics: modelling outbreaks in humans, animals and plants

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ABSTRACT

The 1918 influenza pandemic is one of the most devastating infectious disease epidemics on record, having caused approximately fifty million deaths worldwide. Control measures, including prohibiting nonessential gatherings as well as closing cinemas and music halls, were applied with varying success and limited knowledge of transmission dynamics. One hundred years later, following developments in the field of mathematical epidemiology, models are increasingly used to guide decision making and devise appropriate interventions that mitigate the impacts of epidemics. Epidemiological models have been used as decision making tools during outbreaks in human, animal and plant populations. However, as the subject has developed, human, animal and plant disease modelling have diverged. Approaches have been developed independently for pathogens of each host type, often despite similarities between the models used in these complementary fields. With the increased importance of a One Health approach that unifies human, animal and plant health, we argue that more inter-disciplinary collaboration would enhance each of the related disciplines. This theme issue consists of two volumes and presents research articles written by human, animal and plant disease modellers. In this introductory article, we compare the questions pertinent to, and approaches used by, epidemiological modellers of pathogens of humans, animals and plants, and summarise the articles in this theme issue. We encourage future collaboration that transcends disciplinary boundaries and links the closely related areas of human, animal and plant disease epidemic modelling.

KEYWORDS

mathematical modelling; human disease; animal disease; plant disease; public health; interventions; One health

1. INTRODUCTION

The field of epidemiological modelling is centuries old [1–10]. However, in the past 20 years, modelling has increasingly been used to advise policy during outbreaks [11–16].

Models can be used to forecast the total number of cases (e.g. [17]), as well as to inform intervention strategies (e.g. [11,18]). Recent examples of real-time modelling during outbreaks can be drawn from diseases of humans (e.g. the outbreak of Ebola virus disease in West Africa from 2013-2016 [17,19–22]), animals (e.g. the 2001 and 2007 Foot-and-Mouth Disease epidemics in the UK [11,12,23,24]) and plants (e.g. the invasion of the UK by *Chalara fraxinea*, which causes dieback of ash trees, in 2012 [25]).

Although there are scenarios in which a specific modelling approach is required for pathogens of a particular host type (see section 2.3), there are also many similarities between human, animal and plant disease systems that suggest that common modelling frameworks can be extremely useful. There are important questions that are of interest in all three fields, such as: how can models be parameterised using data collected during an epidemic? How can uncertainty in the data, or in the estimated values of model parameters, be represented in model outputs and then communicated to decision makers? And how can interventions be introduced to fulfil a particular objective – such as to minimise the number of hosts ever infected or reduce the ecological or economic impacts of an epidemic?

As a result of these shared questions of interest, we contend that increased collaboration between modellers across human, animal and plant disease epidemiology will be beneficial and allow modelling approaches to be optimised. In this theme issue, we therefore present articles written by scientists working at the forefront of epidemiological research for human, animal and plant systems. There is a focus on the links between these topics, thereby encouraging future collaboration and cross-fertilisation between these areas.

In this introductory article, we summarise the shape of the epidemiological modelling landscape (Section 2.1) and note that epidemiological modellers most frequently focus on pathogens of humans. We describe some of the types of data available for quantitative analysis of infectious disease epidemics (Section 2.2), as well as the methods used to analyse those data and to represent the dynamics of outbreaks (Section 2.3). We discuss the use of infectious disease modelling to guide forecasting and control (Section 2.4). Throughout, we highlight articles in this theme issue and more widely in the literature. Finally, we provide an overview of this theme issue (Section 3), as well as propose a unified approach involving mathematical epidemiologists focussed on pathogens of humans, animals and plants to be used going forwards (Section 4).

2. MODELLING EPIDEMICS IN HUMANS, ANIMALS AND PLANTS

2.1 Shape of the modelling landscape

The field of epidemic modelling is dominated by studies of human diseases, with commercially-important livestock disease modelling second. Models of plant disease outbreak dynamics are less numerous, despite the economic impacts of plant pests and diseases [26] as well as their effects on biodiversity [27] and ecosystem services [28].

In 2015, the journal *Epidemics* published a range of articles describing outstanding challenges in modelling infectious disease dynamics [29], including challenges in modelling for public health policy [15], modelling livestock diseases [30] and plant disease modelling [31]. As an illustration that epidemic modelling is dominated by studies of pathogens of humans, however, in the 92 articles published in *Epidemics* since 2015, we find that two thirds (61) of articles were on human diseases (Fig 1A). Of the other articles, 16 were on animal (mainly livestock) or fish diseases, 11 on general methods that can be applied to a range of systems and four on zoonotic infections. In the last two years, there were no papers at all in that journal on plant disease modelling.

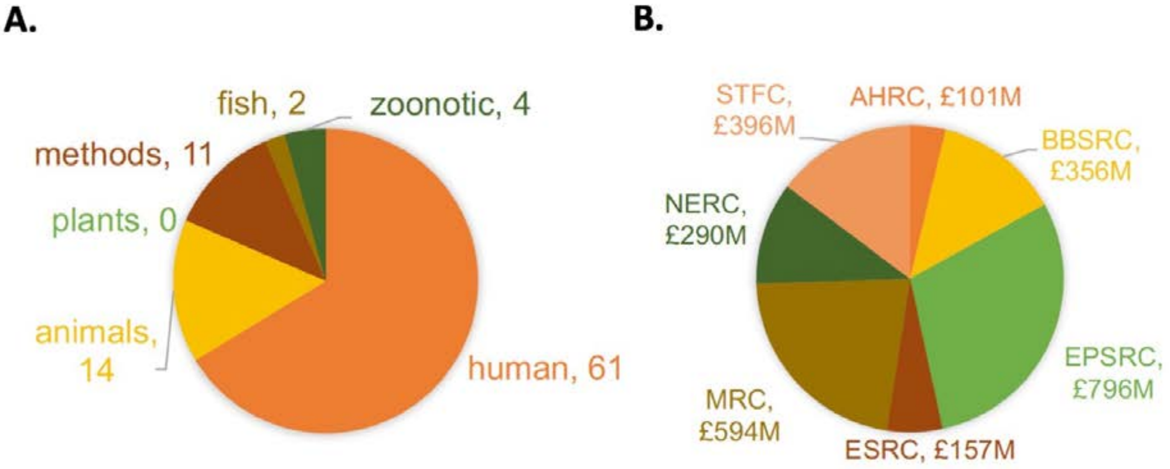

Figure 1. Most epidemic models represent outbreaks of pathogens of humans, rather than plants or animals. A. The topics of published studies in the epidemiological modelling journal *Epidemics* between 2015 and 2019. B. The annual funding provided to the research councils that fund epidemic modelling by the United Kingdom government. More funding is directed towards funders that support modelling studies of pathogens of humans rather than plants or animals.

Similarly, there have been theme issues of *Philosophical Transactions of the Royal Society B* since 2016 on topics such as the 2014-16 Ebola epidemic [32], marine diseases [33] and the concept of One Health [34]. Yet, despite some theme issues [35] containing studies about plant diseases [36,37], no theme issues exclusively about this topic – and about plant disease modelling in particular – have been compiled.

Despite the overall focus on public health and modelling pathogens of humans (and animals, to a lesser extent), there are a number of research groups working in plant disease epidemic modelling. As described below, these groups have tended to publish their research in journals specifically focused on plant systems such as *Phytopathology* [38–40], *Plant Pathology* [41–43], and *New Phytologist* [44,45], rather than more general (and typically higher impact) journals, with a few high profile exceptions (e.g. [46,47]).

The dominance of human disease modelling is driven by several factors. First, the availability of funding (Fig 1B). In the United Kingdom in 2017/8, the Medical Research

Council received more than one and half times more funding (£594 million) than either the Biotechnology and Biological Sciences Research Council or the Natural Environment Research Council, both of which fund animal and plant disease modelling. Human disease modelling is also funded by a number of charitable foundations including the Wellcome Trust. Charities such as the Bill and Melinda Gates Foundation provide funding for animal and plant disease modelling (e.g. the project on West African Virus Epidemiology for Root and Tuber Crops), however they fund epidemiological studies of human pathogens to a higher extent.

Second, there is a wide range of journals that publish human disease modelling studies, and they tend to have higher impact factors. While top-tier general interest journals do accept impactful modelling studies, more specialist journals of veterinary epidemiology or plant disease, for example, tend to be lower impact than human epidemiological journals. As a result, modellers might choose to focus on human diseases. This is despite the huge impact of animal and plant diseases. For example, the annual cost of grain diseases alone in the United States has been estimated at five billion US dollars [48]. To counter this, new plant-focussed journals from high profile publishing organisations, such as the journal *Nature Plants* that was released in 2015, have begun to redress this balance by providing a high impact destination for publishing a limited number of plant disease modelling studies (e.g. [49]). However, it is still the general trend that journals that publish analyses of epidemics in human populations tend to have higher impacts.

2.2 The data revolution in epidemic modelling

The availability of diverse and detailed data has transformed epidemic modelling over the past few decades. Early models developed to capture the epidemiological dynamics of pathogens of humans, such as the Susceptible-Infected-Removed (SIR) model and its approximation applied to plague in India [8], were parameterised using data on the numbers of cases or deaths observed in each time period, and relied on simplifying assumptions about features such as host mixing within populations. Other studies were informed by epidemiological data such as seroprevalence surveys [50]. While simple models are powerful, more complex models require detailed data regarding, for example, the distribution of hosts in the landscape (Fig 2A) or data on numbers of incident cases of multiple pathogens over long timescales (Fig 2B). Multi-annual data for measles provided an early example of the richness contained in many real datasets [51], and these data are still being used to understand transmission dynamics: for example, in this theme issue, Noori and Rohani investigate the interaction between childhood diseases using data dating back to 1904 [52].

Other types of data, such as genomic data (Fig 2C), are now used with models for outbreak investigation [53] or to infer epidemiological links [54]. Although genomic data are most commonly available for human diseases (e.g. [55–57]), in this issue we also have examples of using genomic data to understand the spread of avian influenza in wild bird populations [58,59].

Equally important in models are the assumptions that define the demographic processes of a population. A diverse range of large-scale datasets are being repurposed to understand the interactions that lead to transmission. For example, mobile phone data have recently been used to identify travel patterns to inform epidemiological models [60,61]. In this issue, we have examples of a range of data types being used to direct model development, such as the use of census data to predict emergence sites of imported pathogens [62], data on global travel being used to consider the likelihood of a large-scale pandemic in the modern day [63], and animal movement data being used to predict pathogen spread [64]. There are challenges to re-purposing data: Chaters *et al*. [64] describe methods for using sparse routinely-collected data to define high-dimensional network models.

Perhaps most pertinent for plant diseases given the central role of environmental conditions in determining when new infections are possible, high resolution climate data are becoming increasingly essential for capturing the impact of environmental changes on outbreak dynamics [65]. Bebber [66] uses hourly microclimate data to describe the invasion of black sigatoka disease in banana plants. Chaloner *et al.* [67] discuss the challenges of resolving the spatiotemporal scales of climate data with host data for septoria leaf blotch disease of wheat. We hope that these illuminating examples will lead to a more widespread interest in plant disease modelling among other epidemiological modellers.

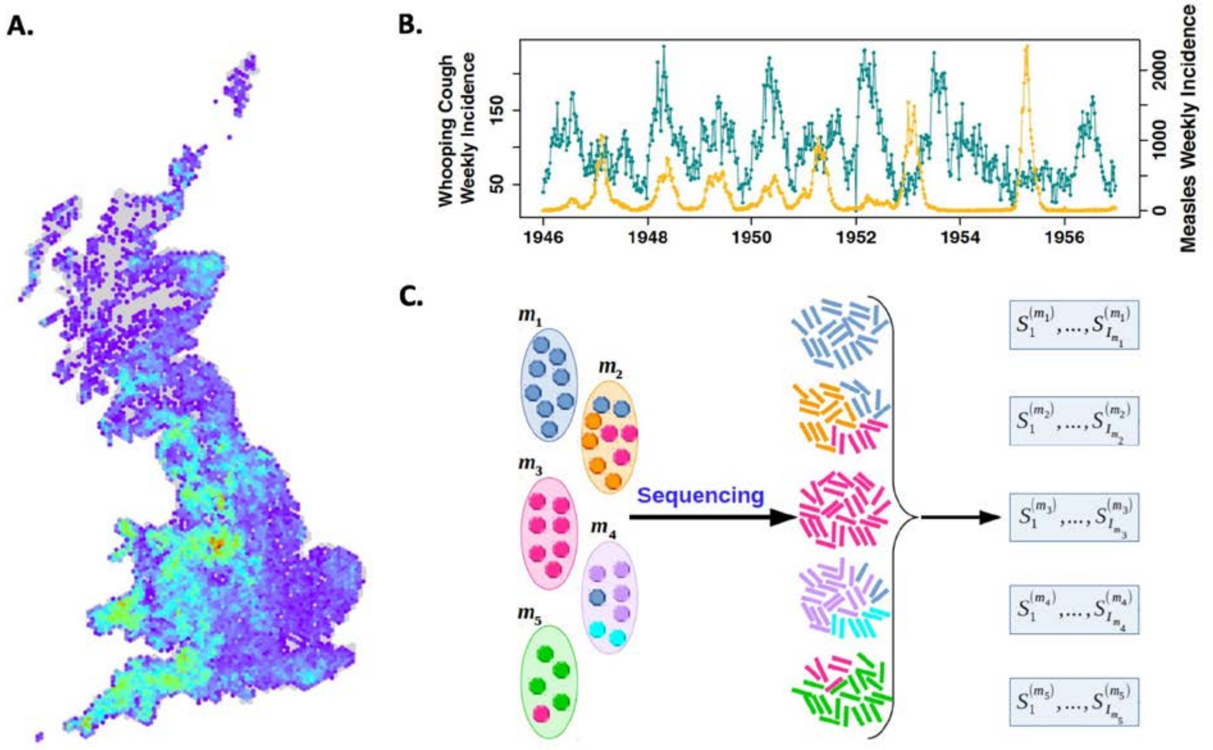

Figure 2. Different types of data can be used to parameterise epidemiological models. A. Data on the locations of hosts in the landscape (here the density of cattle in the United Kingdom, adapted from [64] – see that paper for further details). B. Data on the numbers of new cases in each time period (adapted from [52] – see that paper for further details). C. Schematic showing how pathogen sequence data are recorded from hosts (adapted from [54] – see that paper for further details).

2.3 Types of modelling approach

The most commonly used epidemiological modelling approach is compartmental modelling [68]. Compartmental models can be either deterministic or stochastic, and individuals are categorised according to their infection [69] or symptom [70] status. At the beginning of this theme issue, Kleczkowski *et al*. [69] provide an overview of compartmental modelling, predominantly focusing on the commonly-used SIR model (Fig 3A). This framework has been extended to include a range of epidemiological features, including transmission between hosts via vectors – which is the route of transmission for a number of pathogens of humans, plants and animals. In this theme issue, Alonso *et al*. [71] consider a complex compartmental model of malaria that accounts for features such as superinfection of human hosts, and Chowell *et al.* [72] use a model including pathogen transmission via mosquitoes to consider the impacts of hurricanes on epidemic dynamics.

As well as being able to address questions that are common to diseases of humans, plants and animals, compartmental models can account for differences between systems comprising these different host types. As an example, cryptic infectiousness has been included in plant disease models to represent the fact that some hosts become infectious before the onset of symptoms (see [73,74] and Fig 3B top), whereas simple models of Ebola virus disease in humans have incorporated the onset of infectiousness following a non-infectious but symptomatic period (see [75,76] and Fig 3B bottom).

There are a number of other differences between human, animal and plant disease systems that require different epidemiological modelling approaches. Perhaps the most obvious of these is host movement. Plant populations are typically stationary and livestock are contained within strict boundaries, whereas humans have significantly more freedom of movement which permits long-distance pathogen transmission. However, plant hosts can be motile – for example in plant trade networks – and animal movement underlies the spread of a number of pathogens. Transmission of plant pathogens is also possible via the dispersal of airborne spores over long distances [77,78]. Accordingly, epidemiological models of humans, animals and plants often include a spatial component. In this issue, there examples of spatial livestock disease models based on cattle movements [64], a spatial model of wildlife rabies [79] and spatial models of huanglongbing disease of citrus plants [16,62] (see e.g. Fig 3C). There are also models of epidemics in human populations that illustrate the importance of spatial processes for reproducing real-world observations [63,80,81].

Aside from compartmental modelling, other approaches are commonly used to analyse epidemic data. Renewal process models are often used to characterise the numbers of cases of disease (see e.g. [82]), and statistical models are used for forecasting numbers of cases [83] or representing other processes such as disease surveillance [84]. In this issue, Bourhis *et al*. [85] link a statistical approach for estimating infection prevalence to the Susceptible-Infected compartmental model to account for temporal variations in the number of infected hosts during an outbreak.

The wide range of available models reflects the increasing number of data sources described in the previous section. For example, analyses of pathogen sequencing data have been linked with models of epidemic dynamics leading to the field of phylodynamics [86,87]. This issue includes a review paper by Lycett *et al.* [59] in which the history of avian influenza is summarised, including the inference of transmission routes using phylodynamic methods (Fig 3D).

Such a wide range of modelling approaches provide a suite of techniques for forecasting and planning control when epidemics are ongoing.

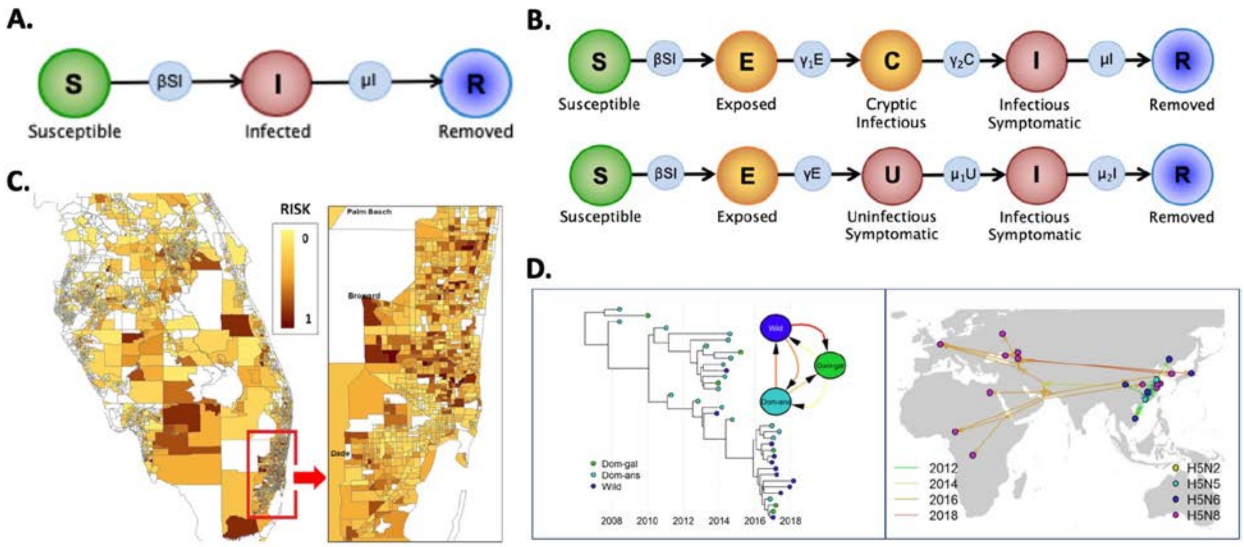

Figure 3. Different types of epidemiological modelling approach can be used to analyse epidemic data. A. Schematic of the classic Susceptible-Infected-Removed (SIR) compartmental model, in which individuals are classified according to their infection status. B. Adapted compartmental models to include infectiousness prior to symptoms (SECIR model – see e.g. [73,74]) or infectiousness after symptoms (SEUIR model – see e.g. [75,76]). C. A spatial model for predicting the risk of introduction of citrus greening (huanglongbing disease of citrus) in Florida in 2010 (adapted from [62] – see that paper for further details). D. Phylodynamic and phylogeographic methods can be used to infer transmission routes (adapted from [59] – see that paper for further details).

2.4 Forecasting and control

As described in the Introduction, mathematical modelling is increasingly used in real-time when epidemics are ongoing for forecasting (Fig 4A) and testing interventions (Fig 4B). This has led to the field named ‘outbreak analytics’ in the context of pathogens of humans [53,88]. Whilst this term has been introduced for human diseases, there are key challenges common to any infectious disease epidemic.

Disease modelling often starts before a pathogen has entered a new population. Risk maps of potential introduction sites can be produced (see the submission to this theme issue by Gottwald *et al.* [62]), and these can in turn be used to guide where to target surveillance. Having decided where surveillance should be focused, it is also necessary to decide which diagnostic method to use. Detection is key in the early stages of an outbreak. Mastin *et al.* [89] present a framework for comparing different approaches for pathogen detection early in an outbreak, and show that visual detection might be the optimal approach for sudden oak death in the United Kingdom.

During the initial phase of an outbreak, once the pathogen has been detected in the host population, a challenge is forecasting whether initial cases will fade out or whether they will go on to spark a major epidemic [75,90]. This question is common to pathogens in a range of systems. Using pandemic influenza an example, Thompson *et al.* [63] consider the probability of a major epidemic when a pathogen arrives in a population following a prior epidemic of a related pathogen, but also notes examples such as the plant pathogen *Podosphaera plantaginis* [46] to which their conclusions might apply.

Once an outbreak has started, it is necessary to estimate its current size from the often limited available data. Bourhis *et al.* [85] demonstrate how the current outbreak size can be estimated from periodically sampled data. Such data might most commonly be derived from animals and plants that are regularly checked for infection, however these data might also be obtained when surveillance takes place at regular intervals during an epidemic in humans (e.g. village visitations to identify Ebola infections in rural areas where access to healthcare is limited [91]). A key parameter for assessing the current outbreak size early in an epidemic is the sensitivity of surveillance, which is also important at the opposite end of the epidemic for predicting whether or not the epidemic has finished once the final symptomatic infectious cases appear to have been safely removed, as demonstrated in this theme issue in the context of Ebola epidemics [91].

Once a major epidemic is ongoing, modelling is used to forecast the total number of cases and to plan how and when to intervene [18]. Gaydos *et al.* [92] show how participatory modelling can be used for forecasting and control, using any of a number of possible types of model from conceptual models to spatial stochastic simulation models. Using stochastic simulations to assess the impact of existing interventions on epidemiological dynamics often involves exploring epidemiological dynamics with and without a proposed control strategy - a problem considered by Lessler *et al.* [93]. Potential interventions include prophylactic controls such as vaccination, considered in the context of wildlife rabies by Baker *et al.* [79] and Ebola in humans by Getz *et al.* [80], and movement bans, an intervention assessed in the context of livestock diseases by Chaters *et al.* [64]. Probert *et al.* [94] and Bussell *et al.* [95] also focus on using models to guide interventions, using reinforcement learning and optimal control theory, respectively – and these approaches could also potentially apply to pathogens irrespective of the type of host.

In any single study, the models used for forecasting and guiding control described here have tended to focus on a specific plant, animal or human disease system. However, there has been recent interest in considering entire systems holistically [34], rather than focussing solely on a limited number of interactions, which might improve forecasts and assessments of the impacts of interventions.

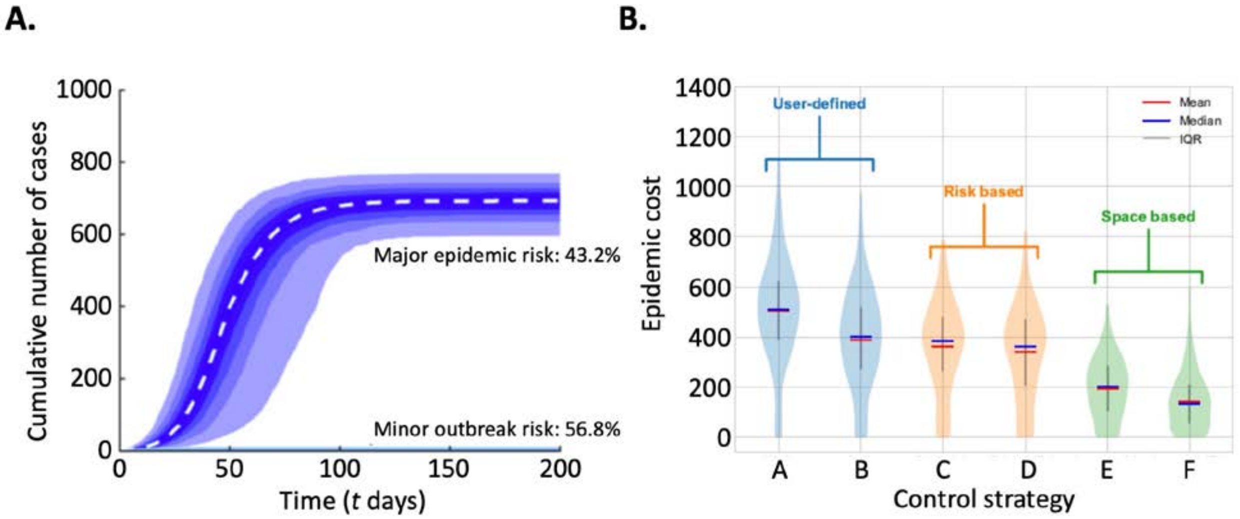

Figure 4. Forecasting and control. Epidemiological models can be used during an outbreak to: A. Forecast whether or not a major epidemic is going to occur and predict the total number of cases (adapted from [63] – see that paper for further details); B. Assess the likely impacts of an epidemic under different possible control interventions (adapted from [95] – see that paper for further details).

3. SUMMARY OF THE THEME ISSUE

To encourage collaboration between modellers of infectious disease epidemics in human, animal and plant populations, in this theme issue we present articles from researchers from across these fields.

This issue is split into two volumes. In the first volume, papers have been contributed that include commonly used methodological approaches and explore important themes in mathematical epidemiology. Methods include compartmental epidemiological models (see e.g. [69,80]) and phylodynamic/phylogenetic analyses (see e.g. [58,59]). Important themes include interactions between different pathogens [52] or different strains of the same pathogen [63], and the impact of weather or climate on the dynamics of epidemics in human and animal populations [72,96] as well as plant populations [65–67].

In the second volume, the main focus is on how epidemiological modelling can be used in real-time during an outbreak. This includes the use of modelling to guide surveillance [62] or assess the vulnerability of a population to disease [97] just before an outbreak has started or early in an outbreak [85,89], and the use of modelling for forecasting or control [16,79,92,94,95] once a major epidemic is ongoing. There is also a contribution about using models to determine when an epidemic has finished [91], as well as articles by public health decision makers about the role of quantitative approaches to guide outbreak responses [53,88].

4. OUTLOOK

In the modern world, over a century after the devastating 1918 influenza pandemic, mathematical models are frequently used as a tool for understanding infectious disease outbreak dynamics and guiding responses to epidemics in human, animal and plant populations. A number of recent advances, such as the availability of increasingly detailed datasets (e.g. whole-genome sequences available in real-time during epidemics) and increases in computational power, are generating opportunities for understanding epidemics in more detail than ever before.

This theme issue brings together research in the fields of mathematical epidemiology for human, animal and plant systems. Given the large number of questions of interest in common to modellers of epidemics in these different host types, we contend that increased collaboration will aid efficient development of methods applicable across these topics, even if certain aspects of specific models must be conditioned to the particular system being considered.

Increased modelling capabilities have been recognised by decision makers, who have recently begun to turn to modellers when epidemics are ongoing. One of the first uses of epidemic modelling to guide interventions in real-time occurred during the 2001 Foot-and-Mouth disease epidemic in the United Kingdom [11,12,23]. More recently, initiatives such as the Centers for Disease Control and Prevention Predict the influenza season challenge [98] and the RAPIDD Ebola forecasting challenge [99] have sought to bring together decision makers and mathematical modellers, particularly during epidemics in human populations. There has also been significant attention directed at epidemic modelling recently, with the television documentary *Contagion! The BBC Four Pandemic* [61] raising public awareness in the United Kingdom, as well as events such as the 30th anniversary of World AIDS Day. There were also a number of journal highlights and special issues marking the centenary of the 1918 Spanish influenza pandemic, including a special issue of the journal *Annals of Epidemiology* [100] and a web focus of the journal *Nature* [101].

Not only might increased collaboration lead to modelling approaches that can be used to represent the dynamics of outbreaks in human, animal and plant populations, but it might also facilitate a ‘One Health’ approach to infectious disease management [34]. Such an integrated approach, in which multiple disciplines are considered and included in a single framework, has been widely advocated as an opportunity for improving outbreak control, with a particular focus on epidemics of zoonotic diseases [102].

Collaborative research therefore has the potential to further improve understanding of epidemic dynamics, and lead to enhanced surveillance, forecasting and disease management in future epidemics. We contend that the need for a unified approach involving modellers from the complementary fields of human, animal and plant disease epidemiology is central to this.

5. EDITORS’ BIOGRAPHIES

Dr Robin Thompson in a Junior Research Fellow at University of Oxford, UK. His research involves using mathematical models to represent the epidemiological or evolutionary dynamics of infectious disease outbreaks in human, animal or plant populations. This includes using statistical methods to estimate parameters associated with pathogen transmission and developing stochastic or deterministic models for generating outbreak forecasts. These forward projections can be used to predict the effects of proposed control interventions. Robin has developed models for a range of infectious diseases in human and plant populations – including Ebola virus disease, HIV, sudden oak death and citrus greening. He also recently developed a method for determining the optimal time to introduce control of an invading pathogen, with applications to diseases of livestock.

Dr Ellen Brooks-Pollock is a lecturer at the University of Bristol. She is interested in applying mathematical modelling and data science to applied questions in the control of infectious diseases. She has spent a lot of time thinking about tuberculosis (TB) in humans, bovine TB in cattle and zoonotic TB transmission from cattle to humans, but is also branching out into Hepatitis A, influenza and vaccination strategies. Ellen has spoken about bovine TB on BBC 1’s Countryfile and BBC Radio 4’s Farming Today and sits on the Editorial board for Mathematics Today.

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COMPETING INTERESTS

We have no competing interests.

DATA ACCESSABILITY

This article has no associated data.

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