Principles of epidemiological modelling

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Summary
Epidemiological modelling can be a powerful tool to assist animal health policy development and disease prevention and control. Models can vary from simple deterministic mathematical models through to complex spatially-explicit stochastic simulations and decision support systems. The approach used will vary depending on the purpose of the study, how well the epidemiology of a disease is understood, the amount and quality of data available, and the background and experience of the modellers. Epidemiological models can be classified into various categories depending on their treatment of variability, chance and uncertainty (deterministic or stochastic), time (continuous or discrete intervals), space (non-spatial or spatial) and the structure of the population (homogenous or heterogeneous mixing). The increasing sophistication of computers, together with greater recognition of the importance of spatial elements in the spread and control of disease, mean that models which incorporate spatial components are becoming more important in epidemiological studies. Multidisciplinary approaches using a range of new technologies make it possible to build more sophisticated models of animal disease. New generation epidemiological models enable disease to be studied in the context of physical, economic, technological, health, media and political infrastructures. To be useful in policy development, models must be fit for purpose and appropriately verified and validated. This involves ensuring that the model is an adequate representation of the system under study and that its outputs are sufficiently accurate and precise for the intended purpose. Finally, models are just one tool for providing technical advice, and should not be considered in isolation from data from experimental and field studies.

Keywords
Disease – Epidemiology – Model – Policy – Principles – Simulation.

Introduction

In animal health, policy decisions regarding the control of infectious diseases often have to be made despite an imperfect understanding of how interactions between agent, environment and host-level factors affect the transmission of infection and development of disease. Epidemiological disease models offer a means to address these uncertainties by combining available information from field and experimental studies and the opinion of experts to gain insight into the dynamics of infection and disease control.

This paper describes the principles of epidemiological modelling for animal health policy development. It reviews some of the uses of models in animal disease management, briefly discusses different modelling approaches, outlines stages in model development, describes some of the considerations that should be taken into account in designing a model, and provides guidelines for the critical evaluation of models.

What are epidemiological models?

A model is a representation of a physical process or system that is designed to increase appreciation and understanding of that system (41). Models are developed in order to understand the effect of external influences on outputs, through representation of the interactions between the components of the system, and to communicate ideas about the behaviour of the system (24, 40).

Epidemiological models are usually defined as mathematical and/or logical representations of the epidemiology of disease transmission and its associated processes (6). In relation to the management of animal diseases, 'models' can be defined more broadly, to include a range of statistical/mathematical tools that look at other aspects in addition to disease spread (6). For example:

– population dynamic models: used to study changes in the structure of a population

– risk models: which describe qualitatively or quantitatively the risk of introduction of disease into a population

– analytical models: used to identify associations between occurrence of disease and risk factors

– economic models: which consider economic values and allocation of resources.

Here the focus is on epidemiological (disease spread) models. By combining available knowledge and expert opinion about a disease, epidemiological models can be used to study complex disease processes, predict patterns of spread under different conditions and evaluate intervention strategies, including novel approaches. They can be a cost-effective way of assessing disease transmission and the effect of different control measures and are especially valuable when there is limited practical experience with the disease of concern.

Why use epidemiological models?

From an animal health perspective, epidemiological models have a range of applications. They can, for example, be used to:

– study disease processes (34, 39)

– generate hypotheses (which can then be used to direct further studies) about factors involved in the persistence of endemic diseases in populations (5)

– provide advice on risks associated with foreign animal diseases and emerging disease threats (3, 27)

– assess the economic impact of diseases

– evaluate control strategies at various scales (2, 13, 16, 33, 44)

– assess the effectiveness of surveillance and control programmes (20, 36, 43)

– provide inputs and scenarios for training activities (19).

Modelling can be particularly useful in cases in which it is impractical or impossible to conduct experimental or field studies (11) or to conduct retrospective analysis of past epidemics to investigate alternative control strategies (30). The use of epidemiological models to direct decision-making during epidemics remains controversial (12), because biological systems are inherently variable and predictions may not be sufficiently accurate or precise for use in the day-to-day management of infectious diseases. Indeed, the use of models as decision support tools in the 2001 foot and mouth disease epidemic in the United Kingdom has attracted much criticism in the scientific literature and popular media (25, 31, 32).

Types of models

Disease models can vary from simple deterministic mathematical models through to more complex spatially-explicit stochastic simulations. The approach will vary depending on how well the epidemiology of a disease is understood, the amount and quality of data available and the background of the modellers involved. The most appropriate type of model to use in a given situation will depend on the sorts of issues being studied and the objectives of the study.

There is no agreed classification system for models. Different authors have focused on different aspects of models which may distinguish them from each other (21, 40). Epidemiological models can be classified depending on their treatment of variability, chance and uncertainty (deterministic or stochastic), time (continuous or discrete intervals), space (non-spatial or spatial) and the structure of the population (homogenous or heterogeneous mixing). Deterministic models use fixed values for parameters and generate a single 'average' or expected outcome, whilst stochastic models incorporate natural variability and uncertainty by including chance elements. Stochastic models, therefore, generate a range of possible outcomes. Time can be represented in models as discrete units or as a continuous process. Continuous time models are computationally efficient but may not realistically represent events that occur irregularly. Discrete time models divide time into equal units and for each time interval the model progressively updates the population status. The choice of an appropriate time unit largely depends upon the dynamics of infection, the quality of data and the level of temporal resolution required. Non-spatial models do not represent spatial relationships between members of the study population. In spatial models, locations or distances are taken into account in disease transmission computations. Finally, models can assume all members of the population are at equal risk of infection (homogenous mixing), or attempt to represent unequal contact between different classes or groups within the population (heterogeneous mixing).

Different modelling approaches are suited to the investigation of different problems. For example, simple deterministic models can be useful for understanding basic infection dynamics but they are of limited use as a predictive tool, since any one epidemic is unique and unlikely to follow an 'average' pattern (15). Stochastic models are more complicated to construct, but are particularly useful for assessing risks and can be used to investigate the likelihood of different outcomes (40). Spatial models can be used to study the importance of geographical factors in the spread of infection and test spatially targeted control strategies, such as contiguous slaughter, ring vaccination and zoning (12).

Traditionally, epidemiological models for animal health have had a strong mathematical basis (21), relying on mass-action or chain-binomial approaches to represent movements of individuals between different disease states. These approaches generally involve fairly simple population structures with homogenous mixing of the population and simplified transmission parameters to represent the spread of disease. Although these types of models have been widely used for studying infectious diseases, they do not necessarily account for spatial, environmental or social dimensions of disease epidemiology. From a disease manager's perspective, outbreaks occur in the context of physical, economic, technological, management and socio-political frameworks. It is well recognised that spatial effects, population heterogeneity and social behaviour can profoundly affect the transmission and persistence of diseases (1, 4, 10, 18, 23, 28), while control of infectious diseases is often a compromise between what is preferable, i.e. large-scale implementation of control measures, and what is logistically or economically feasible (42). There is a growing interest in capturing these complexities in models to better understand the epidemiology and management of diseases (35).

As computing power has increased, more user-friendly programming software has become available, and with greater availability of disease and population data (including spatially-referenced data), the scope and complexity of disease models have increased. Developments in geographic information systems, remote sensing, data analysis methods, network theory and complex systems science are leading to a new generation of epidemiological models. These new approaches include:

– detailed spatial simulation models that consider location, geography and population heterogeneity (6, 11, 19)

– network models that use contact network structures to explicitly capture complex patterns of interaction that underlie disease transmission (1, 7)

– large agent-based models that model a system as a collection of autonomous entities that make decisions individually according to a set of rules and allow for the behaviour of entities to evolve over time (29, 35).

However, the approach taken should reflect the purpose of the study and the type of data available to parameterise the model. Adding complexity to a model may not necessarily improve the quality of outputs (15). The validity of any model ultimately depends on the accuracy and completeness of the data underpinning it (40). Thus, modelling invariably involves trade-offs, both in terms of the complexity versus the availability of data and in specification (i.e. a model that is highly specified for a particular population, time or location may not be applicable to other populations, times or places).

Steps in model building

The authors propose a ten-stage process for developing valid epidemiological disease models (Fig. 1), adapted from the work of Taylor (40), Law (26) and Sargent (38). The ten stages, each of which is described in detail below, are:

– determining the system to be modelled and the objectives of the study

– collecting information and data on the study population and the epidemiology of infection and disease

– developing a conceptual model

– validating the conceptual model

– formulating and/or programming the model

– verifying the model

– assessing operational validity

– analysing sensitivity

– conducting studies

– interpreting outputs and communicating results.

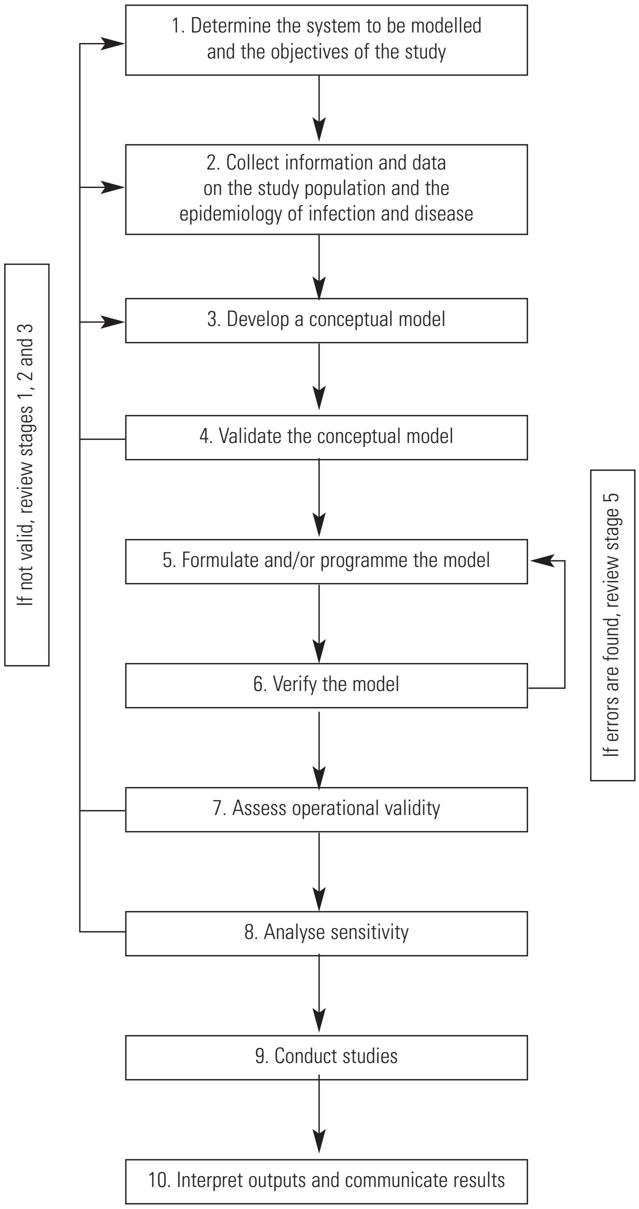

Fig. 1
The process of model development
Adapted from Taylor (40), Law (26) and Sargent (38)

Determining the system to be modelled and the objectives of the study

The first decision to be taken relates to the overall extent and scope of the model. This involves clearly defining the objectives of the study, identifying the system to be modelled and choosing appropriate outputs to monitor the behaviour of the model (26). This stage is fundamental, because the objectives of the study affect the scale, methods, level of detail and the required level of precision and accuracy of a model.

Collecting information and data on the study population and the epidemiology of infection and disease

Reviewing the structure and dynamics of the study population and relevant features of the transmission and control of infection is fundamental to the development of a conceptually valid model (40). This step in model development is analogous to the hazard identification stage of risk analysis, and should aim to develop a list of factors which may affect the accuracy and precision of the chosen model outputs. Once important factors have been identified, relevant data should be collected and analysed to specify model parameters.

This stage can involve the analysis of field and experimental data, literature reviews and/or expert opinion. Collaboration between model builders and subject matter experts (including veterinarians, virologists, microbiologists, agricultural scientists, computer scientists, biostatisticians, etc.) is very important in ensuring that a conceptually valid model is developed (40).

Developing a conceptual model

A conceptual model is a verbal or graphical representation of the system under study (38). Ideally, it should be formulated into a document which describes the chosen modelling method(s), model assumptions and parameter estimates (26). There are many different modelling approaches available to study the transmission of infectious diseases, as discussed above, and the choice of an approach depends upon how applicable it is to the particular problem, the quantity and quality of available data and the skills of the modelling group.

In choosing a particular modelling approach, modellers should consider how to represent the study population, the progress of infection in individuals, the passing of time, spatial relationships, chance, and the transmission of infection. These decisions will also affect the methods used to analyse results from the model. The trade-off between model complexity and data requirements is a common consideration, because data availability and quality is almost always a limiting factor in developing epidemiological models.

Validating the conceptual model

Conceptual model validation is the process of determining whether the theories and assumptions in the conceptual model are appropriate for a model's intended use. One technique is to seek comment on the suitability of its design from subject matter experts. This is known as 'face validation', because it seeks to identify whether a model appears, 'at face value', to adequately represent what is known about the study system (38). If the proposed conceptual model is not valid, then its design should be re-evaluated. Further information and data may need to be collected about the revised processes (26).

Formulating and/or programming the model

The conceptual model is then implemented as a system of equations or as computer algorithms. This can involve the use of:

– a general purpose programming language, e.g. Java (Sun Microsystems Inc., Santa Clara, California, USA) or Visual Basic (Microsoft Corporation, Redmond, Washington, USA)

– scripting languages, e.g. R (R Development Core Team, Vienna, Austria) or MapBasic (Pitney Bowes Business Insight, Troy, New York, USA)

– spreadsheets, e.g. Excel (Microsoft Corporation, Redmond, Washington, USA)

– specific mathematical or simulation software packages, e.g. Mathematica (Wolfram Research, Champaign, Illinois, USA) or @RISK (Palisade Corp., Ithaca, New York, USA).

The choice of software depends upon the design of the conceptual model and the experience of the modellers.

Verifying the model

Model verification is the process of checking that the conceptual model has been adequately translated into formulae or computer code, and that it performs as intended. This may involve structured assessments of the model's logic, formulae or code, and systematically checking the behaviour of internal components of the model (38, 40). If coding or logical errors are found, the model's code or formulae should be revised as appropriate.

Assessing operational validity

The operational validity of a model can be assessed in a number of ways, these include:

– subjective assessments of the model's internal behaviour and results by experts using visualisation or sensitivity analysis techniques (38)

– comparison with results of other models (8)

– comparison of the internal behaviour and results of a model with outcomes of the real system (38).

The latter approach can involve comparing outputs with historical results not used in the development of the model or evaluating the model's capacity to predict the future behaviour of the system (38).

Analysing sensitivity

Gathering quality data to parameterise epidemiological disease models can be challenging, particularly if there is little or no contemporary experience with the disease agent in the study population. In cases where data validity is limited, the importance of uncertain parameters can be assessed by conducting sensitivity analysis studies. Sensitivity analysis involves the assessment of the impact of changes in input values on model outputs (9). A model's input parameters can be varied systematically to investigate how uncertainty and variation in parameter estimates influence outputs (22). If a model's outputs are sensitive to the values of one or more poorly characterised parameters, then the credibility of the model may be enhanced by increasing the precision and/or accuracy of these estimates. Alternatively, user-confidence in a model's results can be increased if its outputs are less susceptible to variations in uncertain parameters.

Conducting studies

The nature of studies conducted depends on the objectives of the model, but often involves investigating the transmission and control of infection under different starting conditions or evaluating factors that lead to endemic infection in different populations. This may involve designing hypothetical model scenarios to investigate the behaviour of the model under certain circumstances.

Interpreting outputs and communicating results

The findings of epidemiological disease models must be interpreted in the context of assumptions made about the behaviour of the system and any limitations of the modelling approach and the quality of data used. It is important that decision-makers and those affected by their decisions understand the use and limitations of the particular model used (24). As a general rule, any direct inferences made from models that have not been fully validated for the current problem should be made with some caution. Even so, results from such models may still be useful to generate hypotheses that can be tested in empirical studies.

Model validation

Models are abstractions and simplifications of the real world and as such the results will always be approximations (14, 24). The key questions of interest to disease managers are: How accurate are models and to what extent do they produce dependable results? The answers to these questions depend on the type of model used and its intended application.

Validation is about assessing the accuracy of model output and ensuring its usefulness and relevance for the intended purpose (37). There are no simple rules to follow when validating models, however, Taylor (40) has identified the following guidelines:

– valid models should make biological sense

– valid models should mimic real life

– valid models should be fit for the use they are designed for

– valid models should not be overly sensitive to the influence of uncertain parameters.

The validity of any model ultimately depends on the accuracy and completeness of the data underpinning it (40). It is unrealistic to expect models to provide accurate predictions of the behaviour of biological systems in the face of incomplete knowledge about the system under study and limited data with which to estimate parameters.

Ensuring a model is valid is a difficult issue if a country has limited or no recent experience with the disease of concern, because it cannot be assumed that the disease will behave in the same way as it has in other countries, given differences in environments, production and marketing systems. One way of increasing end-user confidence is relative validation, where different models are set up to simulate the same scenario, and the outputs compared (8). Consistency in the results of the different models implies that the assumptions taken by each development team make biological sense.

Finally, it is important that decision-makers who use the results of model predictions and those affected by these decisions understand both the advantages and limitations of the modelling approach used (24).

Discussion and conclusions

Epidemiological models are valuable tools that can provide useful insight into a variety of issues associated with the management of animal diseases. To inform policy decisions, models must be fit for purpose and appropriately verified and validated. This involves assessing the accuracy of model output and ensuring its usefulness and relevance for the intended purpose. A model can be considered 'valid' if the data used in its construction are adequate (data validity), its underlying assumptions are considered appropriate (conceptual validity), these assumptions have been correctly implemented as code (model verification), and the model's outputs are sufficiently accurate and precise for its intended use (operational validity) (38). In instances where the validity of data is limited, sensitivity analysis can be conducted to investigate how uncertainty and/or natural variation in parameter estimates or logical assumptions affect the precision of a model's outputs (22).

Models can describe the dynamics of infection and provide a range of possible outcomes, together with estimates of their uncertainty under different scenarios and interventions (17). In managing disease, decisions have to be made in the face of uncertainty, and while epidemiological models can assist in understanding the risks and uncertainties, they should not be considered a substitute for decision-making. Epidemiological models are just one of a number of sources of information available to assist in the decision-making process. Policy-makers should consider results of modelling studies in association with information from traditional epidemiological studies, experimental studies, expert opinion and other sources.

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Les principes de la modélisation épidémiologique

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Résumé
La modélisation épidémiologique constitue un outil précieux d'aide à la conception des politiques de santé animale, de lutte contre les maladies et de prévention. Plusieurs types de modèles sont disponibles, depuis les simples modèles mathématiques déterministes jusqu'aux méthodes complexes de simulation stochastique intégrant la dimension spatiale, en passant par les systèmes d'aide à la décision. La méthode à utiliser dépend de la finalité de l'étude, des connaissances disponibles sur l'épidémiologie de la maladie en question, du volume et de la qualité des données utilisables ainsi que de l'expérience et du parcours des concepteurs du modèle. Les modèles épidémiologiques peuvent être classés en plusieurs catégories, reflétant les différentes approches possibles de la variabilité, du hasard et de l'incertitude (approche déterministe ou stochastique), du temps (temporalité continue ou segmentée en intervalles discrets), de l'espace (approche spatiale ou non) et de la structure de la population (populations homogènes ou hétérogènes). Du fait de la complexité et de la précision croissantes des outils informatiques, et de la perception accrue de la dimension spatiale que revêtent la propagation des maladies et leur prophylaxie, les modèles intégrant les composantes spatiales ont désormais une place prépondérante dans les études épidémiologiques. Les approches pluridisciplinaires recourant aux nouvelles technologies permettent aujourd'hui d'élaborer des modèles encore plus précis pour étudier les maladies animales. Les modèles épidémiologiques de nouvelle génération permettent d'étudier les maladies en tenant compte des infrastructures physiques, économiques, technologiques, sanitaires, de communication et politiques. Afin de veiller à l'utilité réelle des modèles pour l'élaboration des politiques à mener, il convient de les utiliser à bon escient et de les soumettre aux vérifications et validations appropriées. Ces mesures visent à s'assurer que le modèle fournit une représentation adéquate du système étudié et que ses résultats sont suffisamment exacts et précis pour l'utilisation escomptée. Enfin, les modèles ne constituent qu'un outil technique parmi d'autres et ne devraient pas être considérés indépendamment des données fournies par les études expérimentales et de terrain.

Mots-clés
Épidémiologie – Maladie – Modèle – Politique – Principe – Simulation.

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Principios de modelización epidemiológica

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Resumen
Los modelos epidemiológicos pueden constituir una poderosa herramienta auxiliar para la elaboración de políticas zoosanitarias y la prevención y el control de enfermedades. Los modelos pueden ir desde simples y deterministas modelos matemáticos hasta complejas simulaciones estocásticas espacialmente explícitas o sistemas de ayuda a la adopción de decisiones. El planteamiento

utilizado dependerá de la finalidad del estudio, de lo bien que se entienda la epidemiología de la enfermedad en cuestión, de la cantidad y calidad de los datos disponibles y del bagaje de quienes elaboren el modelo. Los modelos epidemiológicos se pueden clasificar en varias clases según el tratamiento que en ellos se dé a la variabilidad, el azar y la incertidumbre (deterministas o estocásticos), el tiempo (intervalos continuos o discretos), el espacio (no espaciales o espaciales) y la estructura de la población (homogénea o mezcla heterogénea). Gracias a la creciente sofisticación de los ordenadores, aunada a la comprensión cada vez más clara de lo importantes que son los elementos espaciales en la propagación de una enfermedad y la lucha contra ella, los modelos que integran un componente espacial vienen cobrando cada vez mayor peso en los estudios epidemiológicos. El uso de planteamientos multidisciplinares, que incorporan todo un repertorio de nuevas tecnologías, hace posible concebir modelos más sofisticados de las enfermedades animales. Los modelos epidemiológicos de nueva generación permiten estudiar una enfermedad teniendo en cuenta el contexto de infraestructuras físicas, económicas, tecnológicas, sanitarias, mediáticas y políticas. Para que resulten útiles a efectos de elaboración de políticas, los modelos deben estar adaptados a sus fines y haber pasado por un oportuno proceso de comprobación y validación. Ello supone tener la seguridad de que el modelo es una representación adecuada del sistema en estudio y de que sus resultados son lo bastante ajustados y precisos para la finalidad que se persigue. Por último, hay que señalar que los modelos no son sino una herramienta para prestar asesoramiento técnico, y no conviene utilizarlos sin tener en cuenta los datos de los estudios experimentales o realizados sobre el terreno.

Palabras clave
Enfermedad – Epidemiología – Modelo – Política – Principios – Simulación.

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