

# Models of macroparasitic infections in domestic ruminants: a conceptual review and critique

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## Summary

A mathematical model is just a means of representing and manipulating something that would not otherwise be accessible. Decision theorists argue that a right decision is one that makes the best use of the available information and using mathematical models of infectious and parasitic disease can help make sure the decision-makers do just that. Seen in this light, models are simply aids to thought – and thus, by definition, good models are useful. This paper deals with the history of mathematical models of parasitic infections of domestic ruminants. It is argued that the early simple forecasting models were very successful, and, although the more complicated models that were constructed to improve the resolution of the forecasts were mostly failures, the experience gained generated a slew of useful, robust models that are still valuable decision-making tools.

## Keywords

Domestic ruminants – *Fasciola hepatica* – Mathematical models – Trichostrongylid nematodes.

## Introduction

The burgeoning interest in mathematical models of the transmission dynamics of nematode and trematode infections of domestic ruminants can be traced back, at least in the English language literature, to a small group of generic, stochastic models (27, 60, 61, 62), and to an equally small group of generic, deterministic models (1, 17, 36, 37). It would make a neat story to suggest that these generic models provided the theoretical basis for the mathematical models that were developed somewhat later to explore the transmission dynamics and control of specific nematode and trematode parasites (e.g. 3, 19, 25, 55) but, with a few exceptions, that would be to ignore what really happened. Although it was eventually realised that within each class of parasites a single generic model framework with suitably adjusted parameter values could satisfactorily represent almost all the infections of interest (50, 51), most of the examples of nematode and trematode models in the literature were constructed on an *ad hoc* basis to address issues dealing with control of a specific parasite in a specific host in a specific country.

A separate, but ultimately converging, modelling thread can be seen in the attempt to create models that predicted (forecast) the incidence of disease – and the concomitant production losses – attributable to nematode and trematode infections of cattle and sheep. In the United Kingdom (UK), this effort began following the catastrophic losses caused by fascioliasis in 1958 (32). In Australia, the focus was on nematodes and the work began a little earlier (18). It continues elsewhere to the present day (e.g. 35).

The history of the last fifty years of modelling nematode and trematode infections in domestic ruminants has been reviewed in detail elsewhere (51, 54). The purpose of the present paper is to describe why it was deemed worthwhile to create models of these parasitic infections in domestic ruminants and to offer a rather general critique of the models that were generated. Illustrative examples will be drawn mostly from the literature on the trematode, *Fasciola hepatica*, but there will be an occasional nod towards the equally important literature on trichostrongylid nematodes. Along the way, I will define what I mean by a 'good' model and parenthetically rebut several misconceptions about modelling, including the notion that

mismatches between model behaviour and the data collected in the field necessarily demonstrate that the model is not 'valid'. Finally, I will describe where I think the models have succeeded and where I think they have failed. It sounds almost superfluous to state that there are good models and bad models, but this needs to be said because there is a growing tendency (especially in the veterinary community) to uncritically assert that all models are bad, especially when used in the face of an actual outbreak (2). Outside of the strictly academic context, models of parasitic infections of domestic ruminants have almost always been created to inform decision-making. This is a difficult task that needs to be approached with considerable care. Nevertheless, I remain an advocate of the utility of models, and I shall repudiate any suggestion that the complicated process of using models to inform decision-making can be reduced to the simple dictum that we should not rely on them too much.

## The characteristics of a good model

A mathematical model is just a means of representing and manipulating something that would not otherwise be accessible. Seen in this light, models are simply aids to thought – and good models are useful. It is worth emphasising here that useful models are not necessarily comprehensive, detailed descriptions of the system of interest. A model can be incomplete, in the sense that it omits some interesting biology, and yet still be useful with regard to the research question the model was created to address. For example, there is a huge literature on the demography and transmission dynamics of the *F. hepatica* miracidium (6, 7, 10, 11, 48, 66), but this larval stage is so short-lived (53), and the consequences of infection so tightly regulated (11), that it has almost no influence at all on the larger dynamics of infection in the mammalian host in which we are usually interested; to understand these dynamics we have to look to the smaller literature on the very long-lived metacercarial stage (e.g. 20, 22, 24, 26, 34, 40, 41, 65). This is reassuring. Parasite life cycles involve so many different processes and are apparently so complicated that we might sometimes be tempted to believe we could never create an entity whose behaviour even approximates that of the system of interest. In fact, we can, and we are able to do so because most of what we see in the field is explicable in terms of just a few very influential processes (49, 56). This rapidly becomes obvious as we move the host/parasite system from the farm yard to the laboratory (4, 50, 51). The biology of the common trematode and nematode parasites of domesticated ruminants is very straightforward and the same wherever you are. What makes the field such a treacherous place to work in is the noise and seasonality

introduced by regional differences in weather and farm animal management practices. All you need to create a useful model for the treatment (say) of *F. hepatica* is a knowledge of the relevant developmental time delays (because strategic dosing protocols exploit these time delays) and an understanding of the biological processes that are the most influential in the regulation and control of parasite abundance (because treatment perturbs the system). If you are interested in effectively forecasting the relative risk of serious fascioliasis you need very much less (as we shall see). Indeed, the activity of modelling is nowhere near as daunting as it might appear to be, especially if we make sure to build a model that is only as detailed as it has to be to provide useful insight into the research question – the ability to do this comes with practice and experience with models, and (crucially) with a very thorough knowledge of the biological literature. The importance of this last point cannot be overestimated.

## Why build models at all?

Historically, there have been four reasons to create mathematical models of parasitic disease in domestic ruminants:

- to predict the occurrence and severity of disease (forecasting)
- to better understand data acquired in the laboratory or the field (analysis)
- to improve upon or buttress advice concerning the frequency and timing of chemotherapeutic and chemoprophylactic drug treatments (analysis and simulation)
- to help explain to farmers (and others) why one treatment protocol might work better than another (education).

### Disease forecasting

It has been known for a long time that the intensity of infection with *F. hepatica* or any of the common trichostrongylid nematodes varies on an annual basis. For many years, parasitologists interpreted these variations, in part, or even largely, as the delayed manifestations of the direct effect of weather on the free-living stages of the parasite life cycle. Because the relevant aspects of the weather were measurable, because their effect was delayed, and because the intensity of infection is one of several factors that have implications for the severity of disease, there were obvious opportunities for disease forecasting.

Gordon (18) established that one could crudely predict the occurrence of nematode infections in sheep using simple

bioclimatograms, but it was in the special case of liver fluke disease, in the UK, that forecasting the distribution and severity of disease became a pressing need that led to a plethora of forecasting methodologies (32). When sheep ingest large numbers of the infective stages (metacercariae) of *F. hepatica*, they are at severe risk of death from the mechanical and other effects of dozens of parasitic larvae tunnelling through their livers on the way to the bile ducts (a condition known as acute fascioliasis). Anthelmintic drugs that kill the larval parasites in the liver were not commercially available in the UK until the late 1960s, a circumstance that proved fatal to tens of thousands of sheep in the catastrophic fascioliasis epidemic that occurred in 1958 (5, 28). Surveys carried out at the time, showed that less than 25% of farmers treated their stock with the dangerous anthelmintics that were available (31) and so the only plausible defence against acute fascioliasis was to remove the flocks to drier and less contaminated pastures before the density of metacercariae became threateningly large. This was inconvenient, costly, and frequently involved land that would, otherwise, have been put to different use. In short, the disincentives to moving stock needed to be balanced by a trusted recommendation that movement was necessary.

Correlational studies, making use of weather records for the years 1727 to 1958, demonstrated that a high incidence of fascioliasis in the autumn was associated with wet summers (29, 33, 59). The role of rainfall seemed simple enough: all the development of the extra-mammalian stages of *F. hepatica* takes place either on the damp habitat of its intermediate snail host or within the snail itself (which aestivates if the habitat dries out). Indeed, there is one stage in the life cycle, the miracidium, for which the presence of soil surface water is an absolute requirement. The snail habitats had to be wet enough and warm enough for long enough to allow eggs in faeces to give rise to metacercariae on pasture (this takes about three months in temperate regions) (28, 43, 44, 58). The forecasting problem was to find an index of soil surface temperature and moisture, that was prognostic of the complete development of the larval parasite stages and which could be calculated sufficiently early that farmers had plenty of time to move their stock. Several such indices (for several parasite species) were created and tested (e.g. 30, 38, 39, 63, 64), but the Mt index was perhaps the most influential. It was simply rainfall less evapo-transpiration, multiplied by the number of rain days calculated for May, June and July (together with a simple adjustment for location). It worked really well (29, 42), even given some failures (21). This rudimentary index of the conditions at the soil surface is still being used (although nowadays the forecast is intended to modulate treatment regimens). The index was successful because it produced simple, regional forecasts of disease incidence (below average, average, above average) that were frequently supported by a surveillance system which

reported on the abundance of the snail hosts (a biological indicator of conditions at the soil surface). It is a paradigmatic example of the judicious use of a model that was only as complicated as it needed to be to produce the required results. Note, for example, that the regions to which the forecasts were applied consisted of large agroclimatic zones comprising several counties. This was seen by some (including myself) as a problem that needed correction and the seductive lure of models that represented the *F. hepatica* system in more detail was that we might be able to predict events on a much smaller regional scale (e.g. a given farm) and to a level of predictive accuracy that would maximise a producer's return on his/her investment in disease control. The 1970s saw a concerted effort to construct more elaborate forecasting models for a whole range of parasite species (see 50 for a review) and the effort continues to this day (3, 12, 13, 15, 16, 35, 50, 68). While all this work has proved extremely valuable in other contexts, I do not believe we achieved very much with respect to forecasting at the level of detail envisaged, although the admixture of parasite ecology and satellite imagery has certainly enhanced our capacity to create regional risk maps (e.g. 23).

Here is the problem. It is completely possible to describe the responses of the free-living stages in the parasite life cycle to changes in temperature and moisture in a laboratory setting (e.g. 9), but there is no way of reliably linking conventional weather data to the detailed microclimate actually experienced by the free-living stages on the pasture surface. For example, the absolute difference between air temperature measured at a height of one metre above the ground surface and the temperature at the soil surface in the vegetation mat is frequently different by several degrees and there is no consistent relationship one with the other (44). Furthermore, the quality of the data we have on the parameters that matter, especially with respect to the more inaccessible infective free-living stages, is very poor indeed. This is particularly true of data derived from the field (56), but the amount of random error that is typical of these systems makes even the laboratory data very difficult to deal with. To make matters worse, the parasite strain for which we do have data (however poor) may be unrepresentative of the strains whose presence we are trying to predict. When it comes to forecasting at the level of detail of the individual farm, the data quality issues seem to me to be insurmountable.

However, the experience gained in trying to improve forecasting models was not wasted and models of the population biology of trematode and nematode parasites have been very useful when providing advice about the frequency and timing of chemotherapeutic and chemoprophylactic drug treatments or explaining the benefits of one treatment protocol over another. These models are dealt with in the next section and, unlike the more detailed forecasting models just described, the class

of models designed to inform intervention strategies has, I think, been very successful indeed.

### **Analysis, simulation and education**

Under this heading, the modelling task, as it has most frequently been presented to me, is as follows:

- to create a model for parasitic infections in domestic ruminants that can be used to design and explain parasite control strategies using short half-life or long half-life drugs that are not equally effective over all age-classes of parasite
- to ensure the model is applicable anywhere that the anthelmintic drugs are commercially available. This means that the model must be able to take account of the different animal rearing and management strategies that one will encounter worldwide, and – almost the same thing – it must be able to take account of the entire range of climatic conditions under which the animals are raised and the parasites occur.

It is important, when presented with a task like that, to have a very clear definition of success before the work begins. Based upon the progress that modellers have made over the last fifty years, here are the feasible components of that definition:

- the model should generate patterns that an experienced field worker would recognise as 'typical' of a given type of farm or ranch in a given agroclimatic area
- the model should not be expected to predict the events on any specific farm in any specific year
- the model should be expected to be able to rank the efficacy of parasite control strategies in order (and to replicate the rank order of strategies already tested in the field).

In answer to the usual question of whether it is even possible to build a model that satisfies these criteria, it is informative to ask what has been achieved in the absence of a formal mathematical framework and why. Novel and effective control strategies have been devised in the absence of mathematical models. This has been possible because much of the complexity of parasitic systems is irrelevant to the task at hand. As we observed earlier, most of what we see in the field can be explained in terms of a relatively small number of population processes. By focusing on these simple conceptual models (which is to say, by thinking very hard about the problem) it has been possible to formulate interventions that work. Mathematical models are feasible for exactly the same reason: we are dealing with a tractably small number of very influential processes that are fairly easily represented in mathematical formulas. Indeed, mathematical models

are ideal mechanisms for representing, refining and testing the reasonableness of the conceptual models (that is, the hypotheses) that constitute the parasitological literature. It follows that we do not need a model which replicates every nuance of the observed epidemiology of the parasite (even if that were possible). But this is not to suggest that simple models are always more useful than complicated ones. Because we build models to address specific questions the model needs to be as complicated as required to address the question posed. But how do we know when it is complicated enough? Even apparently obvious statements, such as: 'If we are dealing with a spatially explicit control strategy such as ring culling we are going to need a spatially explicit model', turn out not to be necessarily true. It is possible to replicate aspects of several of the simpler rules of thumb about spatially explicit control strategies using deterministic temporal models with no spatial component at all. The rather unsatisfactory answer to the question boils down to 'trial and error' and experience of what has worked in the past. Nevertheless, it is always more efficient to start with a simple framework before moving to something more exacting.

The basic model should include all the relevant time delays (i.e. the longest ones), and the biological processes that are the most influential in the control and regulation of parasite abundance. The processes that control parasite abundance include the weather and animal management practices. The weather exerts its influence on the proliferation of the free-living stages of the parasite life cycle through its effect on stage-specific rates of development, mortality and translocation (out of the faeces). Animal management, related to seasonal climatic changes through their effect on the availability of pasture and water, is important because the seasonal nature of calving, lambing and weaning in many systems results in a sudden increase in the number of susceptible, colonisable hosts (37, 49). The direction of the effect of the processes that control parasite abundance is independent of how many parasites there are. This is not true of the density-dependent factors that regulate parasite population abundance through the effect they exert on parasite survival, fecundity or development in the host. These factors depend in some way upon the current or past intensity of infection and operate so as to constrain parasite abundance within the upper and lower bounds that experienced parasitologists regard as 'normal'. Density-dependent factors must be included in any model constructed to evaluate veterinary interventions because they mitigate the effect of treatment.

It is straightforward to put all of these elements together and the literature is replete with successful models of this kind (e.g. 3, 25, 45, 46, 47, 48). As should be obvious, the biological core of such models is usually very simple, what is difficult is implementing the equations in the context of all the animal management systems one may encounter

and mimicking the effect of treatment – especially treatment with long half-life anthelmintics. This is a computational and not an epidemiological problem, but the exacting nature of writing computer code that incorporates the functionality that most users request should not be underestimated.

And then somebody always asks, ‘How do we know the model works?’, which brings us to the vexed problem of ‘model validation’.

## Model validation

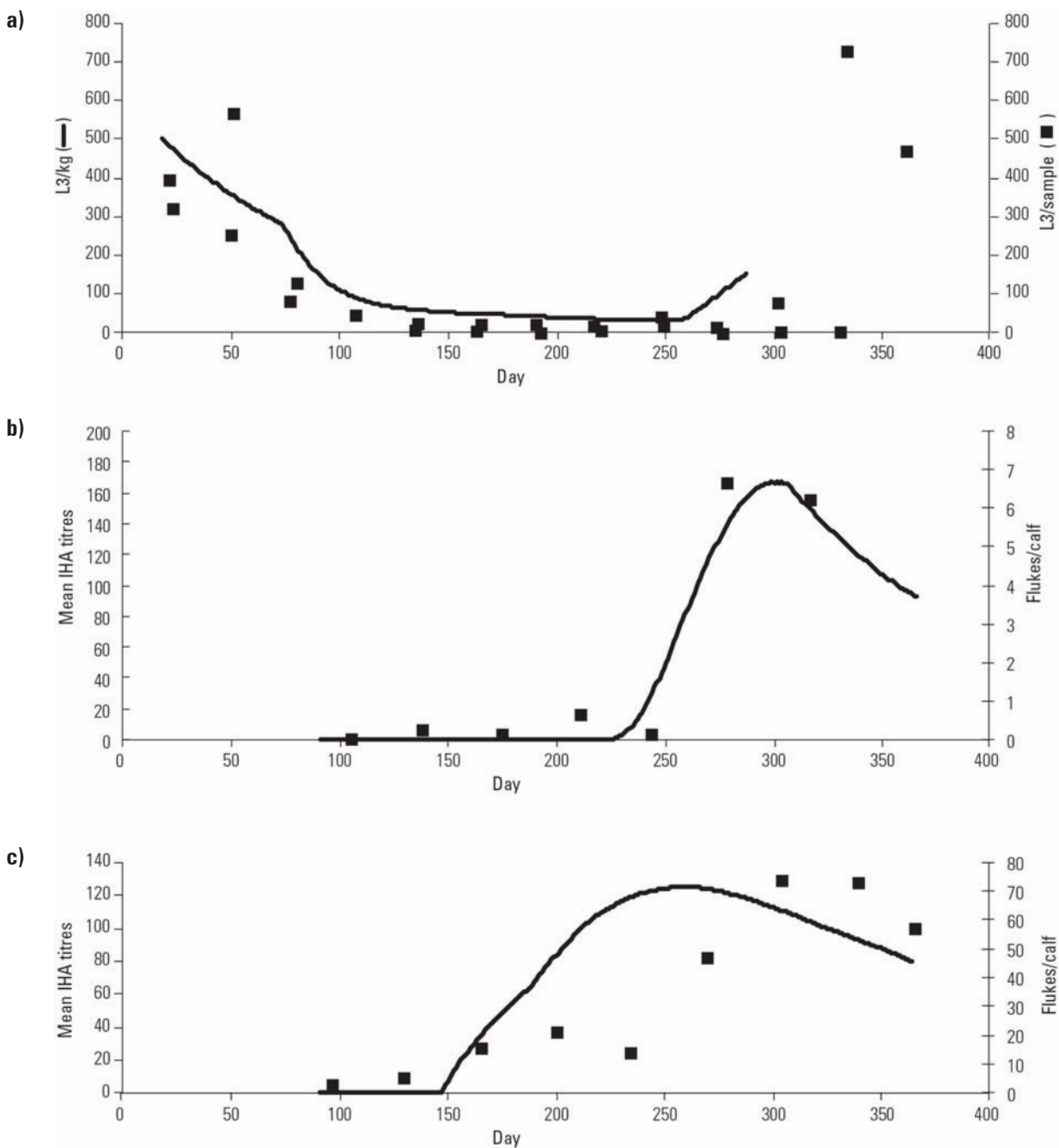
From a modeller’s point of view, one of the most important criteria for validity is whether or not the model was constructed correctly (construct validity). This statement begs the question of what we mean by ‘correctly’, but a more serious objection to this criterion is that it involves technical expertise not often possessed by those who wish to be persuaded that the model is valid. An easy but, in my view, specious response to the question, ‘How do we know the model works?’, is to generate a comparison like that shown in Figure 1. The figure compares the behaviour of models of the transmission dynamics of *Ostertagia ostertagi* and *F. hepatica* with field data on parasite abundance. In Figure 1a and 1b the simulations appear to track the actual observations with astonishing faithfulness, but notice that in both cases the units in which the field data are reported are quite different from the units used to report the results of the simulation. The simulations track the relative changes in abundance very successfully, but the simulated results are coincident with the observations only because of a judicious choice of ranges for the left and right axes. There is, in fact, no evidence at all that the models faithfully track absolute abundance. Furthermore, one can never be certain that even the temporal match between data and simulation is not simply a matter of luck. The coincidence of observations and simulations is crucially dependent, for example, on the initial conditions (e.g. the number of infective stages on the pasture and the prevailing temperature and soil surface moisture) and these are data that we almost never have to hand. As Figures 1b and 1c demonstrate, when the model for the transmission dynamics of *F. hepatica* was used to simulate events on the same pasture in the following year, even the temporal correspondence disappeared. Was this because the model did not work or because we were not so lucky with our guess at the initial conditions for the second year? There is no way of knowing, nor, in fact, is it even a reasonable question to ask, because the comparison between model simulations and the data shown in Figure 1 is an inappropriate test of the definition of success.

It was argued earlier that simple forecasting models for liver fluke disease were successful because they generated

regional rather than farm-specific forecasts. The same criterion applies here. Models created to assist in the analysis and evaluation of veterinary interventions need not (and generally cannot) mimic events on any particular farm exactly, but they should most certainly generate the patterns an experienced field worker would regard as typical for the region and farming type of interest. The central problem here is that the only published data available for comparison deal with specific farms. In such cases, we have to decide how typical the farms are. And then, if the farms are deemed to be within the normal range for farms in that area, how much deviation between data and model output will we tolerate before rejecting the model?

There is another problem too. We model what we can count. But what people neglect to mention is that counting is hard and that real data sets are very messy. Data sets, especially data sets from the field, are tangled webs of bias and confounding. Furthermore, in the field, we tend to measure the things that are easy to measure (e.g. egg counts) and are satisfied with ‘relative’ rather than ‘absolute’ measures; and we are almost always trying (and failing) to sample, and estimate accurate means for, populations that are highly overdispersed. Even in the laboratory, counting can be challenging (48), as anyone who has had to count the number of parasitic nematodes contained in a ewe’s abomasum will attest. There is nothing sacrosanct about data. Epidemiological models are summaries of the prevailing hypotheses about a system and these summaries are almost always based on multiple sources of information: quantitative and qualitative, and the educated guesswork that comprises expert opinion. One might argue, perhaps, that there is a sense in which some models may be better overall descriptions (which is to say, summaries) of the system than any individual data set, and it therefore makes little sense to base the validity of a model on the kinds of comparison shown in Figure 1.

It is reasonable to say that an invalid model is not useful by definition and we can note in passing the trivial point that a model can be valid without being useful. But the real problem is that while risk managers will very quickly let you know whether or not the model is useful, it is not at all clear what constitutes a demonstration of its validity. It was recommended above that one component of the definition of success is that the model should generate patterns which an experienced field worker would regard as typical of the region (in the presence and absence of control). I now offer that as a criterion of validity. One of the reasons for this is that a field worker’s judgement of what is typical is based on the totality of their knowledge and experience and not simply on a certain set of data. By basing the assessment of the model on this wealth of experience we escape the tyranny of highly specific – and always hard to interpret – data sets.



**Fig. 1**  
**Comparison between model simulations (solid lines) and observed patterns**

a) Contamination of pasture with third-stage nematode larvae (L3 larvae per kilogram of herbage) in a cow-calf operation in Missouri

b) and c) Fluke burden in calves grazing a specific pasture in the Netherlands in 1987 and 1988, respectively

(In 1b and 1c observed mean indirect haemagglutination (IHA) titres were used as indices of the intensity of infection)

Source: Data from Couvillion *et al.* (8) and Gaasenbeek *et al.* (14). Simulations taken from Smith *et al.* (52 and 57)

A user's confidence in a model frequently has more to do with the characteristics of the modeller than the model itself – something we should never ignore. Building trust in a model requires the modeller to have a strange mixture of humility and confidence; and, as anyone who has tried it can tell you, technology transfer is a painful process. I wrote in the introduction that there are good models (and modellers) and bad ones – and we all make mistakes. I also believe there are situations where models are not useful

because the modelling task exceeds our capacity. For example, any attempt to translate the effect of treatment on parasite numbers into predictable changes in productivity would be extremely difficult, because productivity (like disease) is multicausal (although see 67 for an opposing point of view). Nevertheless, I remain a strong advocate of using models in decision-making and would claim that there are circumstances in which model-generated solutions are the most useful (specifically when presented

with any condition or event that we have not met before). Decision theorists argue that a right decision is one that makes the best use of the available information. I believe that models can ensure that decision-makers do just that, but I also recognise that the decision-makers will have definitions of success that will be different from mine and, sometimes, maybe even often, they will place more stress

on other considerations. They may well decide on strategies that disappoint me – even if we all think the model is right, which is as it should be. Models are just another head at the conference table. They should be paid as much or as little attention as is paid to the other heads at the table, but certainly no less. ■

## Modèles d'infestations par des macroparasites chez les ruminants domestiques : examen conceptuel et critique

G. Smith

### Résumé

Un modèle mathématique est simplement un moyen de représenter et de manipuler une réalité qu'il serait impossible d'appréhender autrement. Les théoriciens de la décision soutiennent qu'une bonne décision est celle qui fait le meilleur usage de l'information disponible ; les modèles mathématiques appliqués aux maladies infectieuses et parasitaires permettent de s'assurer que les décideurs procèdent exactement de cette manière. Dans cette perspective, les modèles permettent simplement de mieux réfléchir ; il en découle que les bons modèles sont par essence utiles. L'auteur décrit l'histoire des modèles mathématiques appliqués à l'étude des maladies parasitaires affectant les ruminants domestiques. Après le succès rencontré par les premiers modèles de facture simple et à visée prédictive, les modèles plus complexes élaborés par la suite pour améliorer la précision des prédictions se sont pour la plupart soldés par un échec ; néanmoins, l'expérience ainsi acquise a permis de mettre au point un grand nombre de modèles robustes qui constituent, encore aujourd'hui, des outils précieux d'aide à la décision.

### Mots-clés

*Fasciola hepatica* – Modèle mathématique – Nématode trichostrongylidé – Ruminant domestique. ■

## Repaso teórico y crítico de los modelos de infecciones macroparasitarias en rumiantes domésticos

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### Resumen

Un modelo matemático no es más que un medio de representar y manejar una realidad que de otra forma no sería posible aprehender. Según los teóricos de la adopción de decisiones, una decisión es correcta cuando permite dar un uso idóneo de la información disponible, y en este sentido los modelos matemáticos que representan enfermedades infecciosas y parasitarias pueden ayudar a quienes deciden a tener la seguridad de que eso es justamente lo que hacen.

Desde este punto de vista, los modelos son simplemente herramientas que ayudan a pensar (de donde se sigue que los buenos modelos son por definición útiles). El autor, tras repasar la historia de los modelos matemáticos de infestaciones parasitarias en rumiantes domésticos, sostiene que los primeros y sencillos modelos de predicción resultaron muy satisfactorios, y que, si bien los modelos más sofisticados que se elaboraron para mejorar la resolución de las predicciones no ofrecieron casi nunca buenos resultados, la experiencia obtenida se tradujo en gran número de modelos útiles y robustos que siguen constituyendo interesantes herramientas para la adopción de decisiones.

#### Palabras clave

*Fasciola hepatica* – Modelo matemático – Nemátodo tricostrongílido – Rumiante doméstico.



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