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Cattle and nematodes under global change: transmission models as an ally

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Abstract

Nematode infections are an important economic constraint to cattle farming. Future risk levels and transmission dynamics will be affected by changes in climate and farm management. The prospect of altered parasite epidemiology in combination with anthelmintic resistance requires the adaptation of current control approaches. Mathematical models that simulate disease dynamics under changing climate and farm management can help guide the optimization of helminth control strategies. Recent efforts have increasingly employed such models to assess the impact of predicted climate scenarios on future infection pressure for gastro-intestinal nematodes in cattle, and to evaluate possible adaptive control measures. This review aims to consolidate the progress made in this field to facilitate further modelling and application.

Achieving effective nematode control in the 21st century

Over the past decades, several aspects of livestock production, their parasites and the host-parasite relationship have changed and arguably more drastic changes can be expected in the next half-century. Gastro-intestinal nematodes (GINs) represent the most prevalent parasites of grazing ruminants and are an important constraint for livestock farming [1]. Infections with GINs impair the health of livestock, but due to intensive chemoprophylaxis clinical infections are rarely observed and nowadays the focus lies mainly on the economic impact of the disease. The future control of these parasites, however, is challenged by several factors such as the development of anthelmintic resistance [2] and

changes in climate and farm management [3]. Current control programmes are still based on transmission and epidemiological patterns that were mapped decades ago. They need to be re-evaluated and adapted in order to maintain their efficacy [4].

Because the host-parasite system is a tight network, impacting factors will often interact, resulting in a complex web of interrelated and sometimes opposing forces. Future control approaches therefore need to be holistic by taking these interactions into account, and for each adaptive change in management the consequences on the whole system need to be considered before intervening [3, 5].

Mathematical transmission models that simulate disease dynamics and host responses have great potential to improve our understanding of parasite epidemiology under changing conditions and to support the implementation of integrated parasite control strategies. This review first discusses current and anticipated trends for both livestock and their GIN parasites while focussing on the underlying drivers of these changes and their interactions, with the aim of explaining how transmission models are an asset in dealing with changing parasite epidemiology, and can form the foundation of sustainable and effective control. Then, an overview of the currently available models for GIN infections in ruminants is given, focusing on cattle, and recent progress in the development and application of transmission models to predict future risks is discussed. Progress in modelling GIN in other host species, such as sheep, is identified

where it can support similar efforts for cattle. Finally, we identify key challenges in the field and suggest ways of addressing them.

Livestock in a changing world: the toll of intensified farming

In the previous century, global livestock production has grown substantially, with increasing numbers of animals reared and enhanced productivity per animal. In more developed regions, cattle farms have disaggregated into specialised milk and beef industries that show 30% higher milk yields per animal and 30% higher carcass weights, respectively, compared to 1960's production levels [6]. However, the high levels of animal performance reached today compromise other aspects of animal production and the resulting asynchrony between animals and their environment also affects animal welfare [7]. On the other hand, modern production systems are more sustainable than historical methods in that their higher efficiency reduces environmental impact per output unit produced [8]. However, the scale of growth and intensification that the industry has experienced takes a significant environmental toll locally and globally. It is common knowledge now that human activity is one of the primary causes of climate change [9], with global livestock production representing 15% of all anthropogenic greenhouse gas (GHG) emissions [10]. The place of livestock in sustainable food production is increasingly questioned due to concerns around food safety, environmental impacts and animal welfare [11], and these factors are likely to be key in shaping future livestock production systems (Box 1). Global demand for livestock products is expected to double by 2050 [10] and the

livestock industry will thus have a continued role in securing the world's food supply, while operating against a background of increased climate variability and ambitious environmental and social goals. Since GINs are a major constraint on production, achieving these goals will logically rely on increasingly efficient parasite control.

Gastro-intestinal nematodes under climate change

There has been an ongoing shift in the focus of health management in livestock production to disease prevention rather than treatment [12]. In the future, infectious disease patterns are also expected to change, but the impact of these changes is difficult to foresee. For cattle, no longitudinal observations on trends in nematode infection levels are available yet. For GIN infections in sheep, some early evidence of changing trends suggests that not only parasite abundance, but also seasonality and spatial distribution are already affected [13]. The two main drivers of increased risks from GINs are anthelmintic resistance and climate change. Interaction between them and other factors that influence parasite epidemiology, such as farm management, make predicting future parasitic disease patterns and designing adapted control strategies even more challenging.

The emerging phenomenon of anthelmintic resistance [2] necessitates urgently adapted control strategies that are effective in limiting production losses, while maintaining the efficacy of available anthelmintic classes in the long term. The keystone of the currently proposed control approaches is therefore maintaining a

significant proportion of the parasite population in refugia (see Glossary), in order to assure the propagation of susceptibility-associated genes to the next generation. Two newly formalised control approaches that are based on this concept are targeted treatments (TT) and targeted selective treatments (TST) [4]. When applying TT, the whole herd is treated based on knowledge of the risk or severity of infection. When applying TST, only those animals in the herd that are thought to benefit the most from treatment are treated, based on indicators related to parasitological parameters (e.g. faecal egg counts), production parameters (e.g. weight gain, milk yield, body condition score or morbidity parameters such as anemia score). Consequently, future advice on worm control is expected to shift to treating selected individual animals rather than entire herds [4]. Although this imperative is currently stronger for sheep than cattle because of the earlier emergence of anthelmintic resistance in the sheep sector, ensuring the future sustainability of anthelmintic use in cattle points to the need to integrate TT and TST into control measures before resistance becomes pervasive. Lessons and approaches from sheep farming can be usefully transferred, with modification, to cattle systems, and modelling can help to support that.

Because climate is, together with farm management, one of the most important drivers of parasite epidemiology, expected climate change scenarios will also have an impact on parasite infection patterns. The effects of climate change on future parasite epidemiology are not straightforward, and can be direct (Box 2) or indirect (Box 3). Interactions between climate change and anthelmintic resistance

or farm management complicate the development of forecasting tools [14]. Increasingly, novel approaches to control, such as vaccination and breeding for resistant hosts, are being integrated to reduce reliance on anthelmintic drugs, adding further interactions to the system and complicating prediction of changes in epidemiology.

Mechanistic models - a tool to support sustainable parasite control

In the field of veterinary parasitology, transmission models that simulate GIN infections have been around for several decades. Given the nature of parasite-host interactions, transmission models are important tools to represent and manipulate such complex processes and interactions. Forecasting, analysing and educating are the key aims that have driven the creation of transmission models that simulate GIN infections [15]. Transmission models enable extrapolation of current knowledge to alternative scenarios, including possible future changes (see above), and across large spatial and temporal scales [16-18], and will therefore be important to understand the impact of anthelmintic resistance and climate change on parasite epidemiology and to facilitate the implementation of sustainable control strategies.

When developing a model, the main criterion in choosing the most appropriate approach should be the aim and intended application of the final model, since models are often unreliable outside their intended use. Compared to empirical models, mechanistic models are better placed to make predictions concerning parasite transmission and disease risk under alternative conditions because

extrapolation is less of a limitation [19]. Mechanistic models, however, require an in-depth understanding of the processes within the system to be modelled and make use of more inputs and parameters because they generally incorporate more biological detail (e.g. [17]). Lack of knowledge and adequate parameter estimates is therefore the primary bottleneck encountered in the development of this type of model [19]. In practice, however, the distinction between empirical and mechanistic models is not always that strict: most empirical models incorporate a certain level of understanding of the system to be modelled and most mechanistic models include and use some kind of empirical information.

In cases where the effect of chance events and the resulting random fluctuations in population dynamics are of interest, stochastic models are applied. Individual based models are a specific type of stochastic model and aim to incorporate variation between individuals by taking specific characteristics of each individual in the population into account. Incorporating variation between individuals in a model will be required, for example, to simulate TST programmes. Stochastic models explicitly recognise the stochastic nature of the infection dynamics and are therefore able to capture a large range of phenomena. They can, however, be computationally intensive and the complexity of such models can sometimes impair the theoretical understanding while mean-field models provide a more tractable solution.

Development of a mechanistic model for gastro-intestinal nematodes

The development of mechanistic models is a continuous and cyclic process (Figure 1). The development process is in general not finished after validating the first model version, but going back to the drawing board and adjusting model structure and/or model parameterisation will likely be the following step. During model development, uncertainty can arise from different sources and, in general, three types of uncertainty must be accounted for: methodological, structural and parameter uncertainty. Bilcke et al. [20] provide a complete review on the types of uncertainty and how to deal with them. Uncertainty further needs to be distinguished from variability. Where uncertainty mainly originates from a knowledge or information gap, random variation originates from the fact that populations are heterogeneous and that differences exist between and within individuals.

Model structure

The first step in creating a mechanistic model is constructing the model's blueprint. This is typically pictured as a flow chart, in which the different model compartments (e.g. parasite life stages) are incorporated as separate entities that are connected. Most models for GINs are life cycle based models that simulate the different parasite life stages during both the parasitic and free-living phases. Decisions concerning the complexity of the model need to be driven by the goal, as well as the available information and its credibility, but the logical approach is to aim for a model that is as parsimonious as possible: a model only needs to be as detailed as required to provide useful insights into the research

question that is investigated [15]. The potential of creating highly complex models is constrained by the available level of understanding and the accessibility of adequate parameter estimates. Moreover, it needs to be noted that the usefulness of increased model complexity is constrained by the availability of adequate data for model input and validation [21], and increased opacity around the key drivers of model output. Drawing general conclusions from complex models may be difficult [22], and uncertainty analysis and validation (see below) should be used to achieve an appropriate level of complexity.

Parameterisation and parameter uncertainty

Several sources can be consulted to obtain values to parameterise the model framework: literature review, experimental work, expert opinion and data fitting. If adequate data are available, a literature review is a logical start, and ideally should follow the principles of systematic review and meta-analysis of parameter values (e.g. [23]). Directly measuring life history traits (e.g. development time from egg to larvae) in laboratory experiments or field trials has the advantage that specific conditions can be created and replicated (e.g. [24]). In some cases, however, parameter estimates cannot be obtained by measuring or observing and alternative methods need to be used such as expert elicitation [25] or parameter fitting. In the latter approach, model predictions are directly fitted to real observations. The parameter value that provides the best fit between predictions and observations is then implemented (e.g. [26]). Parameter fitting is

an example of how the strict distinction between empirical and mechanistic models is often not justified.

Uncertainty derived from parameter measurement errors, absence of data or inability to estimate parameters, is referred to as parameter uncertainty. Further, it might be that available parameter estimates are not always representative for the parasite species or region of interest. Sensitivity analysis and uncertainty analysis are ways to deal with this kind of uncertainty [20]. Sensitivity analysis attempts to identify key influential parameters by determining the change in model output that results from changes in model input, while uncertainty analysis describes the range of potential model outputs together with their associated probabilities of occurrence. Both methods can be used to identify key parameters with a major influence on model output and can be used to guide further efforts to obtain more accurate parameter estimates. A key point here is that, when estimating parameters, bounds of uncertainty in those estimates should be explicit, so that its influence can be tested across a meaningful interval, and parameters ranked by the need for further work to narrow those bounds.

Uncertainty in parameter values can also be incorporated through fuzzy logic, whereby qualitative descriptions of the conditions under which parameter values vary are formalised in a model as logical operators [27-29]. Although confounding the uncertainty related to model structure and to parameter values, and making it difficult to estimate the influence of each separately, this is a useful way of achieving a working model when adequate quantitative data are scarce, yet

plausible boundaries on key parameters can be justified, for example by expert elicitation.

Model validation

An important step in model development is validation against observed data. Different aspects need to be considered when validating a mechanistic model and no absolute criteria exist. What exactly demonstrates a model's validity is a matter of discussion and is rather related to the intended applications and users of the model than to the model itself [30]. The model of Grenfell et al. [31], for example, was not validated against any observations. Later on, the authors argued that whether 'a model is able to generate patterns that would be regarded as typical for a specific region by an experienced field worker', should be a criterion for validity of GIN models [32, 33]. An objective assessment of such a criterion, however, seems to be difficult in practice and for models intended to extrapolate current knowledge to alternative scenarios in less known contexts, it defeats the purpose. Nevertheless, model validation by comparison with field observations is not always straightforward. It is, as Smith and Grenfell [33] stated, often unreasonable to expect precise correspondence between a single set of observations and model output.

Different approaches for objective assessment can be applied for model validation but no single approach is considered as the overall norm [30]. The display of observations together with simulations in time series plots, for example, aims to provide an overview of model performance in a rather intuitive

manner, but can pose difficulties for exact interpretation [30] or can even be misleading (see [32]). Regression analysis of observations versus simulations, and related approaches (e.g. [34]), therefore have great value [17], by providing estimates of model fit that are quantitative and comparable between models. Excessive reliance on a good statistical fit to data, however, should be avoided when such data are scarce or unreliable, since bias or measurement error in the validation data could undermine the credibility of models that otherwise perform well. A common inconvenience of validating mechanistic GIN models with field observations is that it requires data with specific characteristics and a high level of detail. These kinds of data are often not readily available and are rarely collected for the explicit purpose of model validation. Future efforts should integrate theoretical modelling with practical fieldwork in order to avoid that models are used as secondary analysis and to fuel further progress and advances in this research [35].

Agreed criteria for what constitutes an adequate model fit would be useful but are likely to remain elusive, given the above limitations. Model validation should reveal parameters and other elements, for which the state of knowledge is relatively poor, and this should spur further experiments and, where necessary, changes in model structure (e.g. simplification). Building good models is therefore an iterative process, and validation a fulcrum in this process.

Modelling gastro-intestinal nematodes in farmed ruminants: an overview

The first transmission models that describe GIN infections in ruminants were developed during the mid-1960s. Several reviews elaborate on the description of these models and the challenges faced (e.g. [19, 22, 32, 33]), but an easy-to-access overview of the existing models is lacking. Table 1 aims to provide a comprehensive overview of the available mechanistic models for GIN infections to facilitate future model development. Besides models for cattle, also models for sheep and farmed ruminants in general are included here. Compared to sheep, models for nematode infections in cattle have received less attention and focused on only one nematode species, namely *Ostertagia ostertagi*. Future modelling efforts, however, can benefit from advances made in other host species, such as sheep, and in general modeling and computing to make step changes in their application to cattle. Extension beyond GIN, e.g. to lungworm, should also be a future aim.

Following Smith and Grenfell [33], the models were labelled as either generic or specific in Table 1. Authors often described their model in several subsequent papers, therefore an attempt was made to bundle joint papers as much as possible. Likewise, certain models were further developed in follow-up research by extending the framework or sometimes several existing models were combined into one model. Finally, information is provided on whether a model is deterministic, demographically stochastic or environmentally stochastic, whether it as an individual-based model, and whether the publication reports validation against field observations.

Progress in tackling acquired immunity

Incorporating the acquisition of immunity during the course of a GIN infection and modelling its impact on parasite population dynamics remains an important challenge. The fact that it is so difficult to quantify the level of acquired immunity in a direct manner has made it difficult to determine the adequate mathematical incorporation and parameterisation in models. Reliable data that allow quantification of how parameters related to exposure and immune stimulation correlate to consequences of acquired immunity on parasitological parameters (e.g. fecundity), however, are of great value here.

Some recent approaches have specifically focused on the phenomenon and incorporate explicit descriptions of the development of immunity [26, 36, 37]. Singleton et al. [26], for example, simulated the effects of the immune response on parasite length and fecundity using immunoglobulin A (IgA) titres in sheep as a measure of immunity. The model was later modified to an individual based model that allows immuno-genetic variation [36]. Garnier et al. [37] built further on the moment closure approach of Grenfell et al. [38] and fitted their immune response to data of trickle infection experiments. More mechanistic approaches have also made contributions in the efforts to capture the role of acquired immunity [39, 40]. Specific mechanistic understanding and parameter estimation for cattle, however, are not so well developed.

These recent approaches provide promising and innovative ways to incorporate immunity in parasitic disease modelling and future efforts will need to decide between incorporating increasing mechanistic richness in modeling immunity

despite the presence of uncertainty and taking a more phenomenological or heuristic view. A key question here, however, will be whether the empirical relationships used to derive such solutions are robust to capture changing interactions under, for example, management, environment or genetic change.

Modelling gastro-intestinal nematodes under climate change

Several recent modelling efforts have focused on assessing climate driven changes in future parasite risk levels. A detailed mechanistic framework for GINs in ruminants was developed that allows parameterisation for different nematode species and can be used to predict risk levels of GINs on pasture [17]. Accordingly, this model was used to predict trends in infection pressure for *Haemonchus contortus*, *Teladorsagia circumcincta* (in small ruminants) and *O. ostertagi* (in cattle) under future climate scenarios [17]. Others also explored climate driven changes in the dynamics of GIN infections in sheep by using mechanistic models to demonstrate that small changes in climatic conditions around critical thresholds might result in significant changes in parasite burden [41]. However, not only mechanistic models prove their purpose here [16, 18, 42]. Transmission models with a simplified output, for example, allow extension across a large spatio-temporal scale; this approach has been used to predict a prolonged transmission and increased risk levels for *H. contortus* in sheep in the UK and Europe under future conditions [16]. Further, more empirically driven predictions using a threshold model gave new insights into how climate projections will likely affect parasite epidemiology and parasite disease patterns

[18]. For now, few published predictions have incorporated aspects of future changes in farm management [16], despite its clear importance as a player in the driving forces behind parasite risk, and cattle-specific assessments are less developed. This is a task, which is probably more suited to mechanistic models because these generally include a greater deal of detail and complexity in model structure (see also Mechanistic models - a tool to support sustainable parasite control).

Application and implementation of models

Predictive models aim to forecast the occurrence and severity of disease, while illustrative models serve the aims of simulation, analysis and education [15, 22]. The latter are for example used to improve the understanding of the impact of applying different control approaches on infection levels or the development of anthelmintic resistance, often generalising over several systems. Although this categorisation is rather arbitrary, there is a bias in the literature towards illustrative over predictive models. One reason is that the more specific a model, the easier it becomes to demonstrate imperfections through comparison with data from that specific system. Illustrative models side-step this problem by avoiding claims of fidelity to any exact real-world situation. It is important to overcome this bias against models that are capable of being disproven, if the kind of system-specific models needed for detailed decision support are to see the light of day. Modellers should be transparent about the limitations of their models, and end users accepting of the fact that all models are flawed by virtue

that they must simplify reality. Furthermore, more attention must be given to model implementation and integration with farmer decision systems, if the strong scientific foundation for predictive epidemiological models (Table 1) is to achieve its potential for impact at farm level. To date, scientific advances in modelling these systems have arguably made no difference at all to practical parasite control on the ground. A wider skill set and greater commercial sophistication will be needed to leverage the potential impacts of these models more effectively. In very many cases, potentially useful models have been developed but have not made the transition from scientific paper to application in the field, and greater consideration is needed of the reasons for this and how they might be overcome.

Concluding remarks

The major challenge of the coming years for the cattle industry and livestock production in general will be to produce high quality food in a way that is ethically and environmentally acceptable while maintaining economic viability. To maintain or increase the future provision of animal products, the control of GINs will remain important, but is challenged by the need to decrease the use of anthelmintic products while increased climate variability affects parasite epidemiology. Tools that underpin an approach that takes the consequences of each intervention into consideration can support the orchestration of the complex interplay of influencing factors. Recent efforts show that mathematical models can serve their purpose here, as they enhance our understanding of how future annual parasite risk levels will be affected, and could focus chemical and other

interventions more effectively in an increasingly variable environment. Yet, important challenges remain (see Outstanding Questions), with major bottlenecks in the development of transmission models for GIN including the lack of purpose driven data and the fact that acquired immunity is only partially understood. A better and more active integration of modelling with data collection would mean a great improvement in this matter. The potential to access data from high-throughput diagnostics, originally obtained to monitor performance in intensive livestock systems, and the upcoming trend of performing on-farm measurements, further provide important possibilities in solving the issue of data availability and lowering the costs of data sampling. Knowledge transfer between end users and model developers and identification of user needs will also become action points if, in the long run, we want to achieve a more detailed decision support using transmission models for worm control.

Acknowledgements

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Figures

Figure 1. The cyclic process of developing mechanistic transmission models to simulate gastro-intestinal nematode infections.

Additional material (text boxes, tables, and Glossary)

Text boxes:

Box 1. Drivers of change for the cattle sector: parasites in context

Climate change

The vulnerability of cattle to the effects of climate change depends on geographical region and production system [43]. Climate change will affect animals directly, for example by increasing heat stress [3]. Indirect effects, such as changes in farm management practice and infectious disease dynamics, might, however, be more important. For example, under future temperature and precipitation conditions the length of grazing seasons may increase [44], and this could compromise herbage quality and nutrient concentration, constraining host physiology and immunity [5], as well as prolonging parasite transmission seasons.

Environmental impacts and mitigation actions

Imposed rules and legislative measures to achieve environmental goals, and farmers' attempts to mitigate detrimental effects of climate change, will affect

future animal production. Minimising the industry's contribution to climate change through GHG emissions can be decreased by acting on emissions directly or by enhancing production efficiency and thus lowering the emissions per unit of food produced [45]. Intensification can enhance production efficiency and reduce land use requirements [45], even to the point of zero-grazing systems, but the impacts of inputs into those systems such as fertiliser and fuel, and outputs such as slurry, should be integrated into assessments. While the influence of parasites on GHG emissions is likely less than that of nutrition, reducing parasite challenge can provide a tractable means of intervention to mitigate environmental impacts, by supporting productivity and hence decreasing emissions per unit produced [3].

Public awareness and consumer opinion

In affluent western countries, public awareness concerning food production is growing. Animal welfare is an important consideration, and for cows is often connected with outdoor access and ability to graze, which can also affect perceptions of food quality and healthfulness [46]. In many systems, there are trade-offs between behavioural welfare indicators and disease control along the intensive-extensive gradient, which have been poorly quantified and could affect societal acceptance in future, as could changing dietary preferences (e.g. [47]) and concerns over chemical residues. Without a doubt, public opinions will drive farming system change in future, concurrently influencing parasite risks and the legitimate means for its management.

Box 2. Direct impacts of climate change on gastro-intestinal nematodes

Parasite abundance and larval availability are directly affected by climate through the influence of temperature and moisture on development, migration and mortality of the free-living stages. Future climate scenarios predict an increased daily temperature for temperate regions [9], which theoretically can have opposing effects on the different parasite life stages. Higher temperatures will increase the development rate of eggs and early larval stages found in the faecal pat, but they will also increase the mortality of larval stages found on pasture, especially affecting larval survival during winter [14]. The potential of the predicted temperature increase to affect development or mortality, however, varies between different nematode species and, therefore, also the sensitivity of each nematode species to climate change varies [14]. Moreover, it is possible that the short generation time of these parasites allows for rapid evolution of key life history traits. In addition, not only does the threshold for development of the free-living stages differ between nematode species, but also species-specific needs exist for other life history traits, for example egg hatching in *Nematodirus battus* [48], while increased temperature variability can drive increased or decreased infective stage abundance depending on its relationship with important biological thresholds. The moisture level in temperate regions is not currently considered as a limiting factor for egg or larval development as this process occurs inside the dung [24]. However, rainfall impacts larval emergence from the faecal pat on to the herbage [49]. Future predictions report long periods of drought followed by short periods of heavy rainfall, which could lead to

increased egg and larval mortality in desiccated faeces and sudden increases in larval emergence and pasture infectivity [14]. If parasite abundance will in fact increase, it still remains a complex network of parasite population dynamics and interactions that determines whether this will also lead to an increase in parasitic disease risk [3]. Models can be of great value here; Molnár et al. [50], created a model framework that determines the fundamental thermal niche of a parasite and thus allows to estimate parasite fitness under climate change.

Box 3. Indirect impacts of climate change on gastro-intestinal nematodes

Climate change can also indirectly influence parasite epidemiology by affecting farm management, by influencing the development of anthelmintic resistance or by influencing host immunity. If climate change acts as a driver for longer grazing seasons [44] the period of host exposure to GINs is also increased and the number of potential parasite generations per grazing season may be increased, probably increasing the overall pasture infection level [3]. Theoretically, this could lead to more frequent application of anthelmintic treatments and consequently to development of anthelmintic resistance [51]. Moreover, detrimental effects of climate change on larval survival on pasture can diminish the population of GINs in refugia, further driving the development of anthelmintic resistance [51]. On the other hand, decreased larval survival could mitigate the increase of the pasture population described above, decreasing infection pressure and the need to treat. This will only attenuate selection for anthelmintic resistance if changes in epidemiology are recognized (better still predicted) and acted on accordingly.

Climate change can compromise host immunity by negatively affecting the host's nutrition status [52]. Heat stress is associated with decreased feed intake [53] and grassland quality can be negatively influenced by the expected climate conditions [5]. Mitigation of these trends can be expected through certain anticipated adaptations and interventions [54]. For example, if the future implementation of zero-grazing systems in the dairy industry increases to enhance production efficiency and decrease GHG emissions, the risk of pasture borne diseases such as GIN infections will be reduced. The use of zero-grazing systems can, however, increase the incidence of other diseases [55]; moreover, these animals will not have acquired sufficient immunity against GINs, which becomes important when they, for example, are sold to farms that do pasture their animals [3]. The interplay between exposure, immunity and the production cycle is complex and optimising age-related exposure implies fine judgement at farm level, which can be supported by good models.

Tables

Table 1. Overview of different transmission models for gastro-intestinal nematode (GIN) infections in cattle, sheep and ruminants in general that shows the progression made from early to recent models.

Host species	Parasite species	Lifecycle stage modelled	Generic/Specific	Deterministic or stochastic (environmental or demographic)	Individual based model (yes/no)	Original model (yes/no)	Expansion or application of an existing model	Generic/Specific	Validated against field data	Reference
Cattle	*O. ostertagi*	Entire life cycle	Specific	Deterministic	No	Yes	-	Specific	Yes	[56, 57]
Cattle	*O. ostertagi*	Entire life cycle	Specific	Stochastic (environmental)	No	Yes	-	Specific	No	[58-61]
Cattle	*O. ostertagi*	Entire life cycle	Specific	Stochastic (environmental)	No	No	Application of [58-61]	Specific	No	[62]

Cattle	O. ostertagi	Entire life cycle	Specific	Stochastic (environmental)	No	No	Expansion of [58-61]	Specific	Yes	[63, 64]
Cattle	O. ostertagi	Free-living phase (Develoment from egg to L3)	Specific	Fuzzy rule-based system	No	Yes	-	Specific	Yes	[27]
Cattle	O. ostertagi	Free-living phase	Specific	Fuzzy rule-based system	No	Yes	-	Specific	Yes	[29]
Cattle	O. ostertagi	Parasitic phase	Specific	Fuzzy rule-based system	No	Yes	-	Specific	No	[28]
Sheep	-	Free-living phase (Distribution of L3 on	Generic	Deterministic	No	Yes	-	Generic	No	[65, 66]

		pasture)								
Sheep	-	Entire life cycle	Generic	Deterministic	No	Yes	-	Generic	Yes	[67]
Sheep	-	Entire life cycle	Generic	Stochastic (environmental)	No	Yes	-	Generic	Yes	[68, 69]
Sheep	-	Entire life cycle	Generic	Stochastic (demographic)	Yes	Yes	-	Generic	No	[70]
Sheep	-	Entire life cycle	Generic	Deterministic	No	No	Application and expansion of [71]	Generic	No	[72]
Sheep	-	Entire life cycle	Generic	Stochastic (demographic)	Yes	No	Expansion of [73, 74]	Generic	No	[75, 76]
Sheep	-	Parasitic	Generic	Deterministic	No	Yes	-	Generic	No	[77, 78]

		stage								
Sheep	-	Parasitic stage	Generic	Stochastic (demographic)	No	No	Expansion and application of [77, 78]	Generic	No	[79]
Sheep	-	Entire life cycle	Generic	Stochastic (environmental)	No	No	Applications of [68, 69]	Generic	No	[80-82]
Sheep	-	Entire life cycle	Generic	Stochastic (demographic)	Yes	No	Expansion of [73] by combining it with [83]	Generic	No	[39, 41]
Sheep	-	Entire life cycle	Generic	Stochastic (demographic)	No	Yes	-	Generic	No	[84]
Sheep	*H. contortus*	Entire life	Specific	Deterministic	No	Yes	-	Specific	No	[85]

cycle

Sheep	*T. circumcincta*	Entire life cycle	Specific	Stochastic (environmental)	No	Yes	-	Specific	Yes	[86]
Sheep	*T. circumcincta*	Entire life cycle	Specific	Deterministic	No	Yes	-	Specific	Yes	[87]
Sheep	*T. circumcincta*	Entire life cycle	Specific	Deterministic	No	No	Expansion of [87]	Specific	No	[88, 89]
Sheep	*T. colubriformis*	Parasitic phase	Specific	Deterministic	No	Yes	-	Specific	No	[90]
Sheep	*T. colubriformis*	Entire life cycle	Specific	Stochastic (environmental)	No	No	Expansion and application of [90]	Specific	Yes	[91-93]
Sheep	*H. contortus*	Entire life	Specific	Deterministic	No	No	Adaptation	Specific	No	[94]

		cycle					of [89]			
Sheep	*T. colubriformis*	Parasitic phase	Specific	Stochastic (environmental)	No	No	Application and expansion [90]	Specific	No	[95, 96]
Sheep	*Teladorsagia spp., Trichostrongylus spp., H. contortus*	Entire life cycle	Specific	Deterministic	No	No	Application of [71]	Specific	No	[97]
Sheep	*Teladorsagia spp., Trichostrongylus spp., Haemonchus spp.*	Entire life cycle	Specific	Deterministic	No	Yes	-	Specific	Yes	[98]

Sheep	*T. circumcincta*	Entire life cycle	Specific	Stochastic (demographic)	Yes	Yes	-	Specific	No	[99]
Sheep	*Teladorsagia spp., Trichostrongylus spp., Haemonchus spp.*	Entire life cycle	Specific	Deterministic	No	No	Applications of [98]	Specific	Yes	[100, 101]
Sheep	*T. circumcincta*	Entire life cycle	Specific	Stochastic (demographic)	Yes	No	Application and expansion [99]	Specific	No	[102, 103]
Sheep	*T. circumcincta*	Entire life cycle	Specific	Deterministic	No	No	Expansion of [77, 78]	Specific	No	[104]
Sheep	*T. circumcincta*	Entire life	Specific	Deterministic	No	No	Expansion of	Specific	No	[26]

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		cycle								[70]
Sheep	*T. circumcincta, T. colubriformis, H. contortus*	Entire life cycle	Specific	Deterministic	No	No	Expansion and application of [91]	Specific	Yes	[105, 106]
Sheep	*T. circumcincta*	Entire life cycle	Specific	Deterministic	No	No	Applications of [104]	Specific	No	[107-109]
Sheep	*T. circumcincta, T. colubriformis, H. contortus*	Free-living phase (Development from egg to L3)	Specific	Stochastic (environmental)	No	Yes	-	Specific	No	[110]
Sheep	*T. circumcincta*	Entire life cycle	Specific	Stochastic (demographic)	Yes	No	Expansion of [26]	Specific	No	[36]

Sheep	*T. circumcincta*	Parasitic phase	Specific	Stochastic (demographic)	No	No	Expansion of [38]	Specific	No	[37]
Sheep	*H. contortus*	Entire lifecycle	Specific	Stochastic (environmental)	No	No	Expansion of [97]	Specific	Yes	[42]
Sheep	*H. contortus*	Entire lifecycle	Specific	Stochastic (environmental)	No	Yes	-	Specific	No	[16]
Ruminants	-	Entire life cycle	Generic	Stochastic (demographic)	No	Yes	-	Generic	No	[111, 112]
Ruminants	-	Entire life cycle	Generic	Stochastic (environmental)	No	Yes	-	Generic	No	[73, 74]
Ruminants	-	Entire life cycle	Generic	Stochastic (environmental)	No	No	Expansion of [73, 74]	Generic	No	[71]
Ruminants	-	Entire life	Generic	Stochastic	No	No	Expansion and	Generic	No	[113, 114]

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		cycle		(demographic)			stochastic reformulation of [73]			
Ruminants	-	Entire life cycle	Generic	Stochastic (demographic)	No	Yes	-	Generic	No	[115]
Ruminants	-	Free-living phase	Generic	Stochastic (environmental)	No	Yes	-	Generic	Yes	[17]

Glossary

Deterministic model: Model that assumes no variability or randomness and describes what happens on average in the system or process modelled.

Demographic stochasticity: Variability in population growth arising from random differences among individuals in survival and reproduction rates.

Empirical model: Model based on measurements and observations. Empirical models consider correlative relationships that are in line with the current understanding of the system of interest, but without fully describing the system's behaviour. Synonyms: statistical, correlative, or phenomenological models.

Environmental stochasticity: Variability in population growth as a result of fluctuations in external factors such as climate.

Generic model: A generic model provides a framework that aims to assess the general dynamics of parasite infections. Generic models rather consider a group of similar parasites (e.g. GIN) instead of specific parasite species. In general, they do not incorporate excessive amounts of biological detail and their structure is kept rather simple to not obscure key processes, and to ensure general applicability across a range of systems.

Individual based model: Models that assume a heterogeneous population in which every individual of the population has its own characteristics and that tracks the infection process for each of these individuals. Population level effects are explicitly emergent properties of individual-level processes. In contrast to population based models, these models are therefore per definition considered to be demographically stochastic. A synonym used is agent based model.

Mechanistic model: Mechanistic models are based on the current knowledge and understanding of the system of interest and are therefore process-oriented. They consider the mechanisms that underlie the system's behaviour and explicitly describe these. For infectious disease modelling, these models are typically compartmental. Synonyms: compartmental models, process-based models.

Population based model: Models that assume a homogeneous population. They can be either deterministic or stochastic.

Refugia: Proportion of the parasite population that remains unexposed to anthelmintics, which is found in untreated hosts and/or on pasture.

Stochastic model: Model that incorporates the effect of variable events and the resulting fluctuations in the population dynamics, for example environmental variability such as climate, or demographic variability such as death rates.

Specific model: Specific models describe the population dynamics of a particular parasite species and sometimes of a specific region or specific management situations. They often contain a greater deal of biological detail compared to generic models.