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Density dependence and the control of helminth parasites

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Summary

1. The transient dynamics and stability of a population are determined by the interplay between species density, its spatial distribution and the positive and negative density-dependent processes regulating population growth.
2. Using the human–helminth parasite system as an example, we propose that the life-stage upon which negative density dependence operates will influence the rate of host reinfection following anthelmintic chemotherapy, and the likely success of control programmes.
3. Simple deterministic models are developed which highlight how a parasite species whose population size is down-regulated by density-dependent establishment will reinfect a host population at a faster rate than a species with density-dependent parasite fecundity.
4. Different forms of density dependence can produce the same equilibrium behaviour but different transient dynamics. Under-representing the nature and magnitude of density-dependent mechanisms, and in particular those operating upon establishing life-stages, may cause the resilience of the parasite population to a control perturbation to be underestimated.

Key-words: anthelmintics, metapopulation connectivity, overdispersion, parasite transmission, transient dynamics.

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Introduction

Density-dependent processes are believed to be ubiquitous in nature and recognition of their role in regulating population abundance is an integral part of current ecological theory. In intra- and/or interspecific interactions, negative density-dependent processes restrict growth rates at high population densities and help stabilize natural communities. When population numbers fall, restrictions tend to be relaxed, with the ensuing increase in per capita rates of survival and/or reproduction contributing to population persistence and resilience. There is also a growing realization of the importance of positive (facilitating) density-dependence in ecological theory (Bruno, Stachowicz & Bertness 2003). Host–parasite associations provide a unique opportunity to explore the influence of positive and negative feedback mechanisms on population dynamics (Anderson & May 1978; Adler & Kretzschmar 1992; Rosà & Pugliese 2002).

This paper investigates the influence of regulatory processes on the transient dynamics of helminth parasites following a round of incomplete mass drug administration (i.e. with < 100% therapeutic coverage). Mathematical models can provide valuable insights into the dynamics of parasite populations undergoing perturbations due to chemotherapy and can help optimize treatment strategies to achieve programme objectives (Winnen *et al*. 2002; Stolk *et al*. 2003). However, these models should be validated rigorously against follow-up data obtained from treated populations, as on some occasions they have underestimated the rates of parasite reinfection following relaxation of control efforts (Borsboom *et al*. 2003).

The basic reproduction ratio, denoted R_0, of a helminth parasite is the average number of offspring (or of female offspring in the case of dioecious species) produced throughout the reproductive life span of a mature (or

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female) parasite that themselves survive to reproductive maturity in the absence of density-dependent constraints (Anderson & May 1992). However, for parasites with obligatory sexual reproduction, $R_0 > 1$ is a necessary, but not sufficient condition for parasite population invasion and persistence. Because reproduction is itself a density-dependent process (a host must harbour at least one mated female for transmission to occur), both positive (up-regulating) and negative (down-regulating) density-dependent processes must be considered in formulations of reproduction ratios for these parasites (Nåsell 1976; May 1977).

Regulatory mechanisms can act upon any stage of a parasite's life cycle. This paper explores two categories of density dependence: processes that operate upon parasite fecundity and survival of subsequent transmission stages, and those acting upon parasite establishment and survival within the definitive host. Processes which act upon the production and survival of transmission stages encompass all density-dependent mechanisms that occur between the time a female worm has been mated and fertilized and the time the ensuing transmission stages arrive into a new definitive host (e.g. density-dependent fecundity; density-dependent larval development within vectors). These processes are conditional on the worm burden of the host contributing transmission stages to the next parasite generation (the 'transmitting host'). Density-dependent mechanisms which act upon establishing life-stages include all processes affecting the establishment and development of incoming parasites, as well as the survival of established parasites (e.g. density-dependent establishment; density-dependent adult worm survival). It is assumed that these processes are conditional on the number of worms already established in the host exposed to these infective stages (the 'receiving host').

In this paper, we propose that the rate of parasite reinfection will be influenced by whether negative density dependence is acting upon parasite fecundity or parasite establishment, i.e. whether the process in question is conditional on, respectively, the number of worms harboured by either the transmitting or the receiving host. Helminth populations tend to be regulated by multiple density-dependent mechanisms (Basáñez & Ricárdez-Esquinca 2001). For the sake of clarity, the dynamic consequences of either category of density dependence will be explored separately.

Simple models will be developed, motivated by experimental and observational data, and used to investigate the influence of different density-dependent mechanisms on the rate of parasite reinfection following chemotherapy. A variety of examples will be used in order to illustrate the applicability of the theoretical results both within parasitology and in a broader ecological context, as parallels can be drawn between helminth reinfection following chemotherapy and the colonization of fragmented habitats following environmental change.

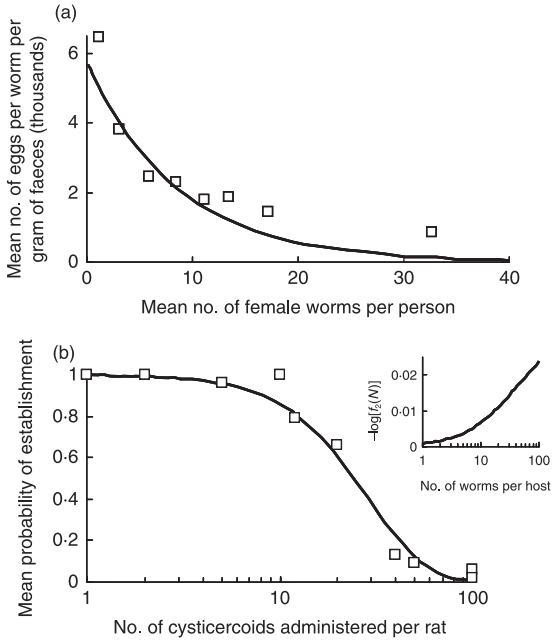

Fig. 1. Density-dependent relationship between transmission process and intensity of infection. (a) Equation 1 was fitted (solid line) to data (open squares) from Hall & Holland (2000) describing the reduction in per capita egg production with increasing number of parasites per host (N) in *Ascaris lumbricoides*, giving $\lambda_0 = 2816$ eggs per worm per gram of faeces, and $c = 0{\cdot}0413$ adult worm^{-1} for density-dependent fecundity. Results are grouped according to mean worm burden. (b) Equation 2 was fitted (solid line) to data (open squares) from Hesselberg & Andreassen (1975) describing the reduction in the number of *Hymenolepis diminuta* worms recovered 56 days postinfection with increasing cysticercoid dose (N), giving $\lambda_0 = 1$, $\sigma = 2$, and $c = 0{\cdot}089$ cysticercoid^{-1} (note the log scale on the x axis) for density-dependent establishment. Graph insert represents the fitted survivorship function as the population's excess worm mortality rate, calculated as $-\log[f_2(N)]$ (Anderson & May 1978; Bellows 1981). Dividing $-\log[f_2(N)]$ by the number of worms gives the additional hazard per individual worm.

Methods

NEGATIVE DENSITY DEPENDENCE

Experimental evidence suggests that negative (down-regulatory) density-dependent mechanisms, operating upon the per capita rate of parasite fecundity and/or establishment, may be adequately described using a negative exponential function, such as:

$$f_1(N) = \lambda_0 \exp[-c(N-1)], \qquad \text{eqn 1}$$

where N is the number of parasites harboured by the host, c is the severity of density dependence and λ_0 is the maximum per worm contribution to transmission when $n = 1$. The decrease in the per worm egg production with increasing worm burden in *Ascaris lumbricoides* (Hall & Holland 2000) is used as an example of a negative density-dependent mechanism acting upon parasite fecundity (Fig. 1a); for a further example in schistosomiasis see Medley & Anderson (1985). Here, λ_0

corresponds to the maximum number of eggs produced per adult female worm per gram of faeces. The exponential expression in eqn 1 can also be used to represent negative density dependence acting upon parasite establishment. Experimental infections with *Strongyloides ratti* in the rat host (Paterson & Viney 2002) have shown that parasite recovery decreases exponentially with increasing infective dose; further examples include *Trichuris muris* in the mouse host (Michael & Bundy 1989) and *Teladorsagia* (= *Ostertagia*) *circumcincta* (= *ostertagi*) in sheep (Grenfell, Smith & Anderson 1987). Here, λ_0 corresponds to the probability of establishment of a single incoming worm. Density-dependent parasite establishment can also be described as a form of density-dependent survivorship, occurring specifically on infective larval stages. Assessing precisely upon which life-stages density-dependent mortality occurs is difficult, even from experimental infections. In the absence of this information, it is assumed that density-dependent establishment acts upon the survival of infective larvae and is conditional on the number of worms co-inhabiting the same host.

The particular shape of the relationship between the parasite density-dependent restriction in question and a host's worm burden may influence population dynamics. The negative exponential expression (Fig. 1a) is compared with another possible functional form (Fig. 1b), which describes a probability of establishment (or survivorship) that is maximal and approximately constant for initial parasite density decaying at an accelerating rate afterwards, i.e. a reverse sigmoid survivorship (Bellows 1981), as recorded in the *Hymenolepis diminuta*–rodent system (Hesselberg & Andreassen 1975). The mathematical expression chosen to represent the reverse sigmoid survivorship is:

$$f_2(N) = \lambda_0 \exp[-c(N-1)]\left[1 + \frac{c(N-1)}{\sigma}\right]^{\sigma}, \qquad \text{eqn 2}$$

where σ is a shape parameter (Fig. 1b). In the limit when $\sigma \to 0$, $f_2(N)$ approaches the exponential function $f_1(N)$ of eqn 1. From now on the expression $f_i(N)$ is redefined as the functions in eqn 1 and eqn 2 divided by λ_0. This allows $f_i(N)$ to have a maximum value of one and separates the density-independent (λ_0) from the density-dependent processes (functions of N) acting on parasite transmission.

PARASITE DISTRIBUTION

Helminth parasites tend to be highly aggregated (overdispersed) among the host population, and the number of parasites per host can be described by the negative binomial distribution (Crofton 1971; Shaw & Dobson 1995). To incorporate the effect of parasite distribution into a mean-based deterministic model, regulation will be modelled within every individual host and then averaged across all possible host infection states (May 1977; Churcher, Ferguson & Basáñez 2005).

In this paper, a composite parameter quantifying the average, per worm regulation of the transmission cycle due to negative density dependence is defined as $\Omega_i(W, k)$, for a given mean worm burden, W, and degree of overdispersion given by the parameter k of the negative binomial distribution; suffix i indicates the particular function, $f_i(N)$ as in eqn 1 or eqn 2. The quantity $\Omega_i(W, k)$ can be calculated as:

$$\Omega_i(W,k) = \frac{\sum_{N=1}^{\infty} P(N) N f_i(N)}{\sum_{N=1}^{\infty} P(N) N} = \frac{\sum_{N=1}^{\infty} P(N) N f_i(N)}{W}, \qquad \text{eqn 3}$$

where $P(N)$ is the probability that a host contains N adult worms. Assuming that $P(N)$ follows a negative binomial distribution, closed forms of eqn 3 can be derived (Appendix S1).

Theoretical work suggests that density dependence may cause a decrease in parasite aggregation with increasing intensity of infection (Quinnell, Medley & Keymer 1990; Galvani 2003). Gathering data from different human communities infected with *A. lumbricoides*, Guyatt *et al.* (1990) used a linear function to represent the relationship between the mean worm burden and the overdispersion k parameter. In our models, it is assumed that parasite distribution changes according to this relationship, although the corresponding parameters were estimated from untreated communities (see Table 1). In addition we assume that there is no latency, i.e. infective stages, once acquired, develop instantly into new adult worms. The implications of relaxing this assumption are discussed later.

POSITIVE DENSITY DEPENDENCE

A type of positive (facilitating) density dependence that must be considered in all dioecious (separate sexes) obligatory parasites is the mating probability. The mating probability, denoted $\phi(W, k)$, indicates the fraction of the female worm population co-inhabiting a host with one or more male worms that is mated. Assuming that the helminth population has a 1 : 1 sex ratio, is completely polygamous, and is distributed among hosts according to the negative binomial distribution with parameters W and k, the mating probability is given by: $\phi(W, k) = 1 - \left(1 + \frac{W}{2k}\right)^{-(k+1)}$ (May 1977).

BASIC AND EFFECTIVE REPRODUCTION RATIOS

In the following, the term 'effective reproduction ratio', denoted R_e, will be used to describe the average number of adult parasite progeny produced during the reproductive life span of an adult worm inhabiting a host population harbouring a given mean intensity of infection, and therefore subject to density-dependent mechanisms. Unlike R_0, R_e is a function of the number of parasites per host at a given time t, reaching unity at

Table 1. Definition and values of parameters and variables used in the model unless stated in the text

Symbol	Definition of variables and parameters	Value and units
$W(t)$	Mean number of adult worms per host at time t	–
W^*	Mean number of worms per host at endemic equilibrium	13¶ host^{-1}
$\Omega_i(W, k)$	Average, per worm down-regulation of transmission; suffix i indicates the functional form $f_i(N)$	–
$f_i(N)$	Density-dependent relationship between the transmission process in question and the number of parasites in a host (N); suffix i indicates the functional form used ($i = 1$: negative exponential; $i = 2$: reverse sigmoid).	–
k	Overdispersion parameter of the negative binomial, assumed to be linearly dependent on the mean number of worms per host, W	$0{\cdot}34 + 0{\cdot}017W$§
R_0	Basic reproduction ratio (estimated from eqn 5)	2·9
c	severity of density-dependent constraint	0·0413¶ worm^{-1}
μ_W	Per capita death rate of adult worms (see Appendix S2)	0·66† year^{-1}
μ_H	Per capita death rate of human host (see Appendix S2)	0·02† year^{-1}

¶Parameterized for *Ascaris lumbricoides* in school-aged children from studies in Nigeria (Hall & Holland 2000). §For *Ascaris lumbricoides* (Guyatt *et al*. 1990). †Anderson & May (1992).

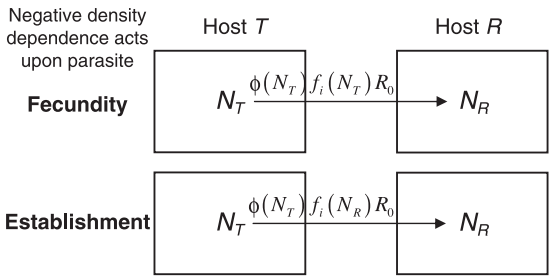

Fig. 2. Flow diagram representing transmission between host T (transmitting host) and host R (receiving host) for the two models under investigation. The two models are identical except for the life stage upon which negative density dependence operates. If population growth is restricted by processes acting upon parasite fecundity, negative density dependence $f_i(N_T)$ will be conditional on N_T, the worm burden of the host transmitting the infection, host T. Conversely, if negative density-dependent mechanisms act upon parasite establishment, $f_i(N_R)$ will be conditional on N_R, the number of worms in the host receiving the infection, host R. Parameter $\phi(N_T)$ indicates the mating probability of a female worm in host T and R_0 is the basic reproduction ratio.

endemic equilibrium (when each female parasite replaces herself and the parasite population size remains constant over time).

Hypothetical helminth species are compared which are identical except for the life-stage upon which negative density dependence operates. When $\Omega_i(W, k)$ is determined by the worm burden of the host transmitting the infection, negative density dependence acts upon parasite fecundity and/or the survival of ensuing transmission stages. Conversely, if $\Omega_i(W, k)$ is conditional on the worm burden of the host receiving the infection, negative density dependence operates upon parasite establishment and/or survivorship. A flow diagram representing the two hypothetical models of parasite transmission under investigation is presented in Fig. 2. All the density-independent processes in the parasite's life cycle have been amassed into the basic reproduction ratio, R_0, which includes the maximum fecundity or establishment λ_0 used previously within eqn 1 and eqn 2. The effective reproduction ratio, R_e, can therefore be written as a function of the density-independent and density-dependent processes in the parasite's life cycle as follows:

$$R_e = R_0[\phi(W, k)][\Omega_i(W, k)] \qquad \text{eqn 4}$$

At endemic equilibrium (i.e. in a stable parasite population before the initiation of any control intervention), the effective reproduction ratio, R_e, will be equal to 1 and therefore R_0 can be estimated by:

$$\hat{R}_0 = \frac{1}{\phi(W^*, k)\Omega_i(W^*, k)} \qquad \text{eqn 5}$$

where W^* denotes the endemic (equilibrium) adult worm burden. In principle, W^* can be estimated from long-term field data and indirect measures of R_0 can thus be obtained (the composite processes included in R_0 are difficult to measure directly).

The expressions for $\Omega_i(W, k)$ and R_0 are used within the model described in Appendix S2 to investigate the rates of parasite reinfection following chemotherapy. For a parasite to be (locally) eliminated, the mean worm burden must be lowered to such an extent that R_e remains consistently below 1. The model is parameterized for *A. lumbricoides* (Fig. 1a), which for moderate levels of transmission reaches an endemic mean worm burden of 13 worms per person, according to Hall & Holland (2000). For a list of definitions, parameter values, and functions see Table 1.

To illustrate the difference between the two categories of down-regulation (acting upon parasite fecundity or establishment), deterministic models were constructed to estimate rates of parasite reinfection following incomplete mass chemotherapy as described in Appendix S2. Typically, mass treatment programmes of human populations achieve, at best, therapeutic coverage levels between 60 and 80% of the total population.

The effects on reinfection rates of the following contrasting scenarios were explored: (1) constraints acting on parasite fecundity were compared with constraints

acting on parasite establishment (the negative exponential $f_1(N)$ function was adopted for both forms of density dependence so that in both cases precontrol R_e profiles are identical); and (2) the negative exponential function was contrasted with the reverse sigmoid $f_2(N)$ function to describe the relationship between density-dependent establishment/survivorship and worm burden. (In both cases R_0 values are the same but the shape of $f_i(N)$ is not.)

In both sets of comparisons it is assumed that the parasite population is at endemic equilibrium prior to treatment and that chemotherapy instantaneously kills all worms inhabiting a treated individual while allowing immediate parasite reinfection (i.e. the drug is 100% efficacious and it has very short half-life within the host). A single treatment is given at year 1 to 80% of the host population. Contact rates with infective stages are approximated by mass action across both treated and untreated sections of the host population. The full models are described in Appendices S1 and S2.

The host immune system is thought to play an important role in mediating many types of density-dependent mechanisms (Tallis & Leyton 1966; Woolhouse 1992; Stear *et al*. 1995; Paterson & Viney 2002). For the purposes of this paper, however, it shall be assumed that all regulation is determined by the current worm load, and not influenced by a host's history of infection. In their study of density-dependent processes during the course of *S. ratti* infection, namely, parasite establishment, survival and fecundity in the rat host, Paterson & Viney (2002) found that not all these processes were affected by the host's previous history of infection, and Woolhouse (1994) refers to some processes affecting *Schistosoma* establishment and fecundity that may not be mediated immunologically. However, and because density-dependent processes with memory are likely to impact parasite population dynamics (Woolhouse 1992), the robustness of the conclusions to adding an immunological memory component into the models will be discussed.

Results

The rate of parasite reinfection after one round of mass chemotherapy, as well as the relationship between the effective reproduction ratio (R_e) and the mean number of worms per host are depicted, respectively, in Fig. 3a,b. In the latter, the R_e profiles are identical for parasites with equally severe density-dependent fecundity or density-dependent establishment. The maximum rate of reproduction per worm (R_{eMAX}), was estimated as 1·8 with the parameter values of Table 1 (Fig. 3b). This value is markedly lower than the corresponding R_0 estimate of 2·9, reflecting the importance of single-sex infections in restricting population growth at low worm densities. The choice of the exponential decay in parasite fecundity or establishment with increasing worm burden accentuates the discrepancy between R_0 and R_{eMAX} and, as the greatest down-regulation of transmission (quantified by $\Omega_i(W, k)$) occurs at low intensities of infection.

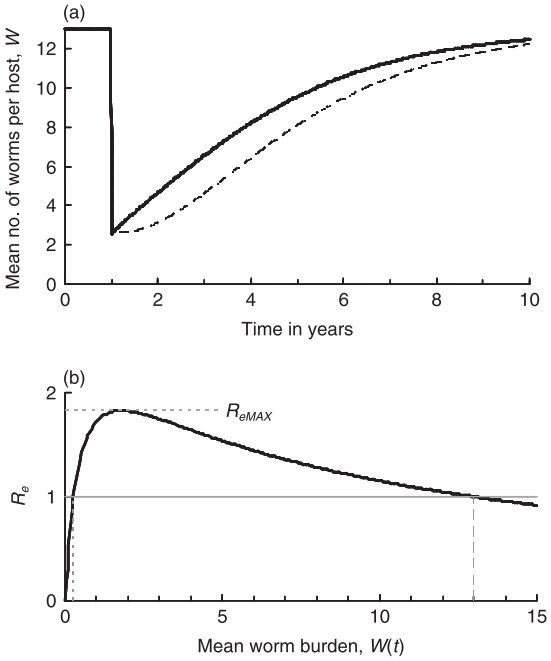

Fig. 3. (a) The rate of parasite reinfection following a single round of treatment given at year 1 to 80% of the host population. The parasite population is down-regulated by either density-dependent fecundity (dashed line) or density-dependent establishment (solid thick line), with identical (exponential) functional forms and parasite values (Table 1). (b) Both hypothetical parasites have identical R_e profiles when both the treated and untreated sections of the host population have the same precontrol mean worm burden. The grey horizontal solid line corresponds to $R_e = 1$, the vertical grey dashed and vertical grey dotted lines mark, respectively, the endemic intensity of infection (W^*) and the breakpoint density; the horizontal grey dotted line indicates the maximum per worm growth rate ($R_{eMAX} = 1{\cdot}8$).

Both profiles cross unity at two intensities of infection: the endemic mean worm burden (the stable equilibrium when $R_0 > 1$), and the breakpoint density (the unstable equilibrium), below which the parasite population will tend towards local extinction (Macdonald 1965; Anderson & May 1992). For a given level of endemicity, parasites with stronger down-regulation or higher parasite aggregation will be harder to control, as they will reinfect a host population faster than those belonging to a species with weaker regulatory constraints (R_0 will have to be higher to compensate for stronger regulatory constraints if the same endemic equilibrium value is to be achieved).

The rate of parasite reinfection will depend on the relaxation of the mechanisms down-regulating transmission, and specifically, on the life-stage whose regulation is being relaxed. Following incomplete mass chemotherapy, a parasite transmitted from an untreated to a treated host will experience very little density-dependent restriction if the negative density dependence operates upon parasite establishment. Female worms in an untreated, heavily infected host will have a high

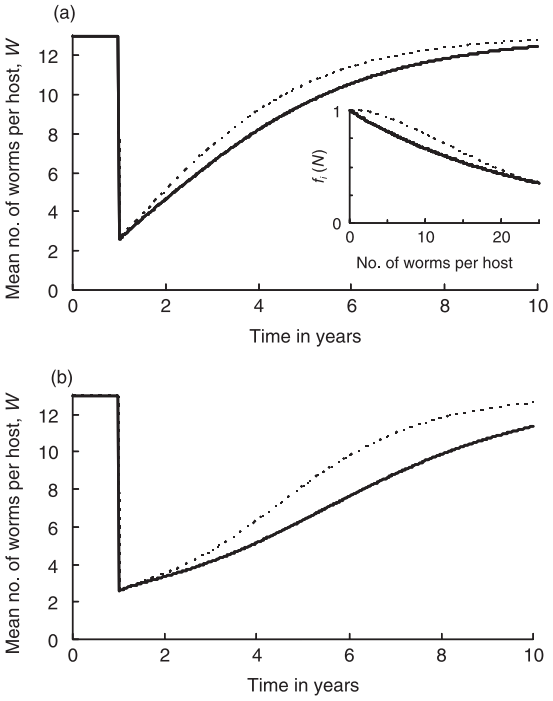

Fig. 4. The impact on the rate of parasite reinfection following anthelmintic chemotherapy of two different functional forms describing the density-dependent relationship between parasite establishment and mean worm burden. The two functions under investigation, namely $f_1(N)$ (solid line, eqn 1, $c = 0{\cdot}0413$ worm^{-1}) and $f_2(N)$ (dotted line, eqn 2, $\sigma = 2$, $c = 0{\cdot}115$ worm^{-1}) are shown in the insert to (*a*). The function $f_2(N)$ was parameterized to allow both parasites to have the same R_0 value of 2·9 and endemic worm burden, $W^* = 13$ worms host^{-1}, yet to differ in density dependence function. In (*a*) the value of the overdispersion parameter, k, follows $k(W) = 0{\cdot}334 + 0{\cdot}017W$ (see Table 1). In (*b*) the degree of overdispersion is considerably lower, $k(W) = 5 + 0{\cdot}017W$.

chance of mating and their offspring will have a high probability of completing their life cycle if transmitted to a treated host where density-dependent constraints on parasite establishment will be minimal. Conversely, if down-regulation operates upon parasite fecundity, a parasite transmitted from a heavily infected untreated host to a treated host would still have the same probability of completing its life cycle as it would have before treatment, because the constraints regulating parasite population abundance will have already operated within the transmitting host.

Therefore, with everything else being equal, a species with negative density dependence acting upon establishing life stages will reinfect the treated section of the host population at a faster rate than a species with density dependence operating upon the production of transmission stages (and hence still acting within the untreated hosts who will constitute the main source of reinfection) (Fig. 3a). This delay in reinfection is accentuated by mating restrictions imposed by single-sex infections, as female worms infecting treated hosts may initially find themselves without access to males. Sufficiently high reinfection rates will eventually enable the worms in the treated host population to exceed their breakpoint density and contribute to transmission.

The rate of parasite reinfection will depend on the interplay between the shape of the functional form chosen to represent density dependence, the intensity of infection, and the distribution of worms among hosts. The insert to Fig. 4a shows the two functional forms under comparison for the rate of parasite establishment. Equation 2 was parameterized to ensure that both hypothetical parasites have the same R_0, i.e. $\Omega_1(W^*, k) = \Omega_2(W^*, k)$. Results are relatively insensitive to whether negative density dependence has the $f_1(N)$ or $f_2(N)$ functional form. However, stronger differences in parasite reinfection would be seen if a high proportion of the host population consistently had a low worm burden, as this is the parasite density at which $f_1(N)$ and $f_2(N)$ and differ most. This is the situation when there is low parasite aggregation (Fig. 4b) or after multiple rounds of chemotherapy (not shown).

Discussion

Population stability depends on the life cycle stages upon which density dependence operates. Using the host–helminth parasite system as an example, this paper has shown that species whose population size is restricted by processes acting upon parasite establishment will be more resilient to control efforts than species constrained by processes operating upon the production and survival of transmission stages. The interplay between multiple opposing density-dependent mechanisms makes the relationship between mean worm burden and transmission highly nonlinear. A similar hump-shaped relationship between survival and population density has been found experimentally in drosophilid flies (Rohlfs & Hoffmeister 2003).

Published estimates of R_0 for gastrointestinal helminths and schistosome parasites tend to be low, typically in the range of 1–5, compared to those of viral infections and filarial parasites (Anderson & May 1992). This would suggest that they should be relatively easy to eliminate, although practical experience indicates this is clearly not the case (Woolhouse, Hasibeder & Chandiwana 1996). Failure to identify and quantify all the positive and negative density-dependent processes governing parasite population dynamics could go some way towards explaining this discrepancy.

Before reliable estimates of parasite reinfection (and their associated uncertainty) can be made, models reflecting the complex biology of human–helminth infections will be required. While addition of greater biological realism such as intrinsic incubation periods, temporal heterogeneity or variable aggregation under control interventions (Anderson & Medley 1985; Quinnell *et al.* 1990) into mathematical models would affect the predicted rates of parasite reinfection, our qualitative conclusions are likely to remain valid. Including, for instance, immunological memory into the model would reduce differences in reinfection rates between parasites

with density-dependent fecundity and those with density-dependent establishment, but the latter will still tend to reinfect a host population at a faster rate than the former. The difference between parasites down-regulated by a process operating upon fecundity or establishment will diminish if the species have long-lived infective stages which persist within the environment, as they will provide a continual source of reinfection.

Most existing models investigating the impact of chemotherapy on helminth infections have been developed by fitting equilibrium data and subsequently predicting the impact of the intervention. At endemic equilibrium, density dependence maintains a constant level of infection over time, irrespective of where upon in the life cycle down-regulating processes act. Although a model may be robust enough to predict the intensity of infection at equilibrium, the crucial regulatory mechanisms may be misplaced within the parasite's life cycle for lack of experimental or observational evidence, the shape of the true relationship misrepresented, or the true magnitude underestimated. This will lead to R_0 values also being underestimated.

The importance of density dependence in helminth population dynamics is widely understood (Duerr, Dietz & Eichner 2005). However, and more importantly, due to the difficulty in obtaining experimental data on the nature and magnitude of density-dependent mechanisms operating upon establishing life-stages (as they occur within definitive, vertebrate hosts), these processes may have been systematically under-represented, causing the resilience of the parasite population to control efforts to be underestimated or at least not adequately quantified. Ideally, the world-wide helminth control programmes now in operation should systematically collect parasite reinfection and abundance data under the pressures exerted during the intervention (Brooker *et al*. 2004). Such data could be used to obtain indirect estimates of the severity of density-dependence acting within definitive hosts by fitting biologically realistic models, which incorporate all those regulatory processes that are directly measurable.

The concepts outlined above can be considered in a broader ecological context. Consider, for example, inter- and intraspecific negative density-dependent mechanisms acting on coexisting species living in assemblages with metapopulation structure. It is well recognised that the stability of a species facing external perturbation or natural variability depends on the degree of connectivity between patches (Ovaskainen & Hanski 2003), in the same way that persistence of a parasite population depends on the intensity of transmission between hosts. The key message of this paper is that a species' stability and persistence will be determined in great measure by whether density dependence acts upon the parent's fecundity, or on the establishment of offspring migrating to less populated patches (where density-dependent competition is relaxed). The importance of distinguishing between these processes should be understood adequately and their magnitude quantified.

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Supplementary material

The following supplementary material is available as part of the online article (full text) from http://www.blackwell-synergy.com

Appendix S1. Derivation of closed forms for $\Omega_i(W, k)$

Appendix S2. Models of parasite reinfection.