Transmission dynamics of *Echinococcus multilocularis* in a patchy environment

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Abstract
We illustrate some of the challenges and potential benefits of modelling parasite population dynamics in a spatially explicit manner, using the example of *Echinococcus multilocularis* in semi-arid areas of Kazakhstan. We show that by taking a parasite-focused approach to modelling population dynamics, rather than the usual host-focused approach, we gain new insights into the complex factors that affect parasite transmission. However, restrictive assumptions are required in order to use RAMAS GIS for modelling parasite ecology. For example, because the host is modelled as habitat, parasite-induced mortality must be negligible. Although these assumptions are probably valid in our case, they are unlikely to apply to many host-parasite systems.

Introduction
There has been an increasing realisation of the importance of incorporating spatial dynamics into models of the transmission dynamics of parasites and infectious diseases, particularly when hosts are free-living in the wild (Mollison & Levin 1995, Hess 1996, Kennedy 2001, Hudson et al., 2002). Spatial variation in parasite prevalences can reflect complex interactions between climatic suitability for free-living stages and host ecology (including host movement patterns, population dynamics and the extent to which primary and secondary host distributions overlap).

*Echinococcus multilocularis* is a tapeworm which has wild carnivores as its definitive hosts and small mammals as its intermediate hosts (Eckert et al. 2001, Fig. 1). It is widespread throughout the Northern hemisphere, and causes fatal disease in humans if eggs are accidentally ingested. In Kazakhstan *E. multilocularis* has been found in 18 rodent species and 4 carnivore species (mostly in foxes). Its prevalence depends strongly on the biome (Fig. 2). This is chiefly because egg survival is strongly related to humidity and temperature (Eckert et al. 2001); under optimal conditions (4°C and high humidity) eggs can remain viable for up to 16 months. Temperatures in desert areas of Kazakhstan can reach 40°C in the summer, with very low humidity; under these conditions eggs are not likely to survive for more than a few hours. Hence extensive field surveys in arid areas of Kazakhstan only found infected rodents in patches with a humid microclimate, such as depressions or river valleys (Shaikenov & Torgerson, 2001). In mountains or river valleys, up to 8% of rodents examined were infected, and around 30% of carnivores. By contrast, in desert areas <1% prevalence was found in both rodents and foxes.
In Kazakhstan’s desert areas, *E. multilocularis* is found in only one rodent species, *Rhombomys opimus*, the great gerbil. This species lives in colonies of 30-40 animals; although overall densities average 7/ha, in favourable locations there can be 2-3 colonies per hectare, leading to substantially higher densities. Each colony forages in an area of radius approximately 40-50m around their burrow. Although *R. opimus* individuals can migrate considerable distances they tend to be sedentary, particularly during the spring and summer. Foxes too are relatively sedentary in March-August while they raise their cubs, and in the desert regions they favour the damper microhabitats where *R. opimus* is found. Foxes migrate long distances in the autumn, and live around human habitations and in wooded and riverine areas in the winter.

Hence in Kazakhstan’s deserts, transmission is most likely in the spring, when both hosts are present and active and climatic conditions are suitable for *E. multilocularis* egg survival. Foxes eat adult rodents infected the year before, then there is a pre-patent period of around a month, after which eggs are excreted to be picked up by a new rodent host. There is only a 2-3 month period in which the climate is equable enough for transmission. There is a lag of several weeks between rodent infection and the beginning of cyst growth, but once cysts start to grow rapidly, they can damage the host relatively quickly (Devouge & Ali-Khan, 1983). Rodents infected late in the season can carry cysts through the winter because low external temperatures retard cyst growth (Novak, 1983). Adult worms do not live for long, so overwintering in foxes is not significant.

**Approaches to modelling *E. multilocularis* dynamics**

Traditional approaches to epidemiological modelling often use compartmental models, with the host as the focus of analysis, and differential equations governing the movement of individuals between susceptible, latent, infected and recovered compartments (Anderson & May, 1991). Models of macroparasites usually also include parasite numbers, either explicitly or implicitly. Roberts (1994) presents a simple compartment model for *E. multilocularis* which includes a parameter proportional to the number of eggs on the pasture and the number of worms in the definitive host. This parameter is used as the explanatory variable in functions describing the rate of acquisition and loss of immunity by hosts. Models of the dynamics of *Echinococcus granulosus*, a closely-related species that cycles between dogs and domestic livestock, have fitted differential equations to data to represent prevalence at age in intermediate hosts. This allows inferences to be made about infection pressure and whether hosts acquire immunity after prolonged exposure to the parasite (Torgerson et al. 1998).

By approaching the problem of modelling *E. multilocularis* dynamics from the RAMAS GIS perspective, we take a very different view of the important features of the parasite’s population dynamics. Because RAMAS only models single species, we focus on the parasite population itself rather than taking the usual host-focussed approach. Because we are interested in metapopulation dynamics within a landscape, we focus on the transitional zone between the wet steppe areas where *E. multilocularis* is found at relatively high prevalence, and the desert areas where it is not able to persist. Hence the habitats of interest are the semi-arid areas where it is found only in rodents inhabiting damper areas such as depressions. By using RAMAS, we could:

- predict conditions for persistence of *E. multilocularis* in marginal habitat (i.e. in areas of desert/semi-desert in Kazakhstan).
• examine the effects of climatic variability on persistence and assess the potential for persistence in desert areas that may be affected by global climate change.
• predict the host communities and vegetation structures where the parasite might be able to persist, and hence help to target control/avoidance measures for reducing human infections.

The parasite population is visualised with cysts as “individuals” within the “habitat” of a sedentary rodent population. The density of the rodent population and the vegetation type determine the carrying capacity and habitat suitability of a patch. Dispersal between patches occurs through rodents being eaten by foxes. The parasite then develops into an adult worm and is transported to other patches by the fox. Fecundity rates are the rate of release of eggs into a patch by the adult worm. Hence the model has three stages; egg, cyst, worm, of which only the worms can disperse and reproduce.

Using RAMAS GIS to model *E. multilocularis*

The data that are currently available are not adequate for model parameterisation. Extensive field surveys are required before the model can be parameterised with confidence, and used to address the modelling aims discussed above (Table 1). Here we present a preliminary illustrative model that gives an example of the dynamics of the system (Table 2). The output from this model is a low and variable prevalence of cysts, with regular metapopulation extinction (Fig. 3). This is in line with our field observations.

**Habitat suitability**

The landscape capability of RAMAS GIS means that we can use maps of rodent densities and vegetation type to determine the number of patches of suitable habitat for the parasite, the suitability of each patch, and so the number of parasite populations that exist in a given area. In our example, we used typical input maps of rodent density and vegetation cover to create a metapopulation with nine patches.

The microclimate in a shaded vegetated area differs substantially from that in surrounding areas, hence the longevity of the free-living egg is influenced by local vegetation type as well as by overall climatic conditions. Because the rodents are effectively the habitat for the parasite, habitat suitability is a function not just of climatic conditions but also of rodent population density. Hence the vegetation type (representing the length of time for which an egg is viable and so available for ingestion by a rodent) and the number of rodents in an area are combined to give a measure of habitat suitability. We model the carrying capacity of a patch for cysts as a non-linear function of habitat suitability. We also make intrinsic growth rate dependent on vegetation type, capturing more directly the relationship between microclimate and egg survival.

**Density dependence**

Because parasites occupy individual hosts, density dependence happens at the intra-host level. Parasites in general tend to be overdispersed in their distributions, so that a few individuals contain large numbers of parasites, and most contain very few. Density dependence takes a number of forms: In definitive hosts of tapeworms in general, the more tapeworms there are in the gut, the fewer eggs each produces (Keymer 1982). In the intermediate host, *E. multilocularis* is unusual among taeniid tapeworms in carrying out asexual reproduction, so that even a single ingested egg can, over time, produce a large number of infective cysts. Complex density dependent processes are likely because an animal with a large number of cysts is both more likely to succumb to parasite-related mortality (reducing transmission rates) and to be preferentially predated (producing inverse density
dependence, and increasing transmission rates). The potential effects of host immunity further complicate the picture.

We cannot model these complexities explicitly. In particular, there is no mechanism for modelling overdispersion because we cannot model individual hosts. A simple population-level representation of density dependence in foxes could be included by assuming that fecundity rates vary with the total number of adult worms, which would be adequate if overdispersion was not severe. However, the literature on the related species *E. granulosus* suggests that density-dependent effects (caused by crowding of worms in the gut or by an immune response) only occur with very high worm numbers and repeated exposure (Gemmell et al. 1986), while Roberts et al. (1995) state that there is no evidence for acquired immunity or parasite-induced mortality in the definitive host for *E. multilocularis*. Hence we do not model density dependence within the definitive host.

In the intermediate host, however, density dependence is important. Cysts continue to grow and multiply in the rodent, causing severe damage and raising host mortality rates (Devouge & Ali-Khan 1983, Schantz et al. 1982). We model density dependence implicitly through the non-linear relationship between habitat suitability and carrying capacity. We also include it explicitly through scramble-type density-dependence, with cyst survival dependent on cyst abundance. This provides a simple population-level approximation to host acquired immunity and parasite-induced host mortality.

**Variability**
The semi-arid areas of Kazakhstan have a highly seasonal and unpredictable climate. There are frequent drought years, and occasional years of very high snowfall. Harsh winters (called *dzhuts*) may cause host mortality, and may affect transmission through changes in host behaviour. Egg survival may also be affected by the weather during the spring. We incorporate stochasticity into the model through variability in carrying capacity, and through occasional catastrophes causing raised egg mortality.

**Dispersal**
The part of the lifecycle that takes place within the fox is modelled through parasite dispersal rate and fecundity. We assume dispersal in rodents is negligible. In order to capture the dependence of fox foraging behaviour on rodent availability, we assume that dispersal is dependent, through carrying capacity, on the number of rodents in the receiving population. Other than this, dispersal is assumed to be distance-related.

Within the spring transmission period, a fox may forage in several neighbouring patches within its home range. During this period the cysts ingested in one patch can develop into adult worms within the fox and release their eggs in another patch. However, in our model we use an annual timestep. Hence the subtleties of dispersal at two scales (within and between years) cannot be captured.

**Management actions**
Because we are dealing with a parasite rather than an endangered species, management focuses on sending the metapopulation to extinction rather than preserving it. The main approach to controlling *E. multilocularis* is using bait laced with the anthelmintic praziquantel. A fox-baiting programme in Europe aimed at *E. multilocularis* used 15 baits per km², and succeeded at reducing prevalence of the parasite in foxes from 24% to 4% (Schantz et al., 1995). We model this using the “harvest” option, assuming that if bait is left in a patch,
a given proportion of the worms in that patch is killed. The increase in extinction risk from baiting in any combination of patches and at different frequencies could then be assessed, and compared to cost data for a full evaluation of a strategy’s cost-effectiveness.

Model applicability
We make a number of assumptions in this study, which may not be generalisable to many other parasites (Table 3). For example, we assume that hosts act as habitat for the parasite and as a medium for dispersal, but that the parasite itself is not a significant driver of host dynamics. We model host dynamics implicitly to some extent, by making parasite carrying capacity and vital rates stochastic and prone to catastrophes (hence mimicking climatic effects on host populations). We model fox foraging behaviour by making dispersal rates dependent on parasite density in the destination patch. But this uses parasite density as a proxy for rodent density, to which it is not linearly related. We also assume that the predator-prey relationship is not intense, so that the population dynamics of each participant is not significantly affected by the other.

These assumptions may possibly be valid in the case of E. multilocularis in the semi-arid regions of Kazakhstan, but not for most multiple-host parasite species. They may also be realistic for directly-transmitted helminths of the gastro-intestinal tract. E. granulosus also exists in an endemic steady state, with no significant acquired host immunity, low reproductive ratios (number of new parasites generated by each adult parasite) and low prevalence (Roberts 1994). Other parasites may be maintained at a low level due to consistently low biotic potential or poor transmission success, for example Oestrus ovis. Parasites can also exist at high prevalence without host immunity, e.g. parasites in the genus Skrjabinema. In cases such as these, the modelling framework we have developed may be applicable.

One of the most interesting features of E. multilocularis in semi-arid areas is its degree of dependence on environmental factors. The potential for parasite transmission is highly constrained by the strongly seasonal climate, and is affected by climatic unpredictability. Transmission can only occur at times when the rodents are active, predators are present and eggs are viable - this narrows the timing down to spring. The presence of patches with a favourable microclimate allows parasites to persist in the desert region. However, these patches of lusher vegetation may also have an important role in host dynamics, which could further complicate the modelling.

We have discussed the potential applicability of RAMAS GIS to the system under study, using an illustrative model. Our approach gives a very different perspective to that normally encountered in the parasite modelling literature. RAMAS allows us to emphasise the under-researched spatial aspects of parasite population dynamics, which makes it a valuable additional tool for parasite modellers. The method used in the programme of scoring patches on habitat suitability could be a useful simplification where several factors important to transmission covary with habitat type. Hence in cases such as E. multilocularis, where these aspects are key components of system dynamics, using RAMAS GIS may produce meaningful conclusions that could be used to drive management interventions.

Acknowledgements
We gratefully acknowledge the financial support of INTAS Project 97-40311 for this work.
References


Table 1 Data needs for model parameterisation.

<table>
<thead>
<tr>
<th>Component</th>
<th>Data required</th>
<th>Use in model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vegetation</td>
<td>Map of vegetation types, including rodent densities and cumulative annual egg viability under normal conditions and in catastrophe years.</td>
<td>Habitat suitability map</td>
</tr>
<tr>
<td>Fox and rodent biology</td>
<td>Rodent densities - mean and variability, how they vary with vegetation type, and how they are affected by catastrophes.</td>
<td>Habitat suitability function, carrying capacity</td>
</tr>
<tr>
<td></td>
<td>Fox densities - mean and variability, and how they are affected by catastrophes.</td>
<td>Dispersal probability</td>
</tr>
<tr>
<td></td>
<td>Fox movement distances - mean, shape of function and how they are affected by catastrophes.</td>
<td>Dispersal distance function</td>
</tr>
<tr>
<td>Parasite biology</td>
<td>Transition probabilities between the three stages - egg, cyst, worm, with associated variability.</td>
<td>Survival probabilities in stage matrix</td>
</tr>
<tr>
<td></td>
<td>Number of eggs produced per adult worm, and effect of population-level density dependence on this.</td>
<td>Fecundity rates, density dependence</td>
</tr>
<tr>
<td></td>
<td>Effect of catastrophes on egg survival, hence on effective number of eggs produced per adult worm.</td>
<td>Fecundity rates</td>
</tr>
</tbody>
</table>
Table 2. Major assumptions made in the example model. The assumptions are presented in the format of the RAMAS summary file, with the inclusion of information about the patch model.

Patch model
Input maps: Vegetation cover, Rodent density
Habitat Suitability = thr([veg],0.2)*[rodents]
Habitat Suitability threshold = 0.2
Carrying Capacity = 10*(1-exp(-0.25*ahs))
Rmax = 1+[veg]

Stages

<table>
<thead>
<tr>
<th>Stage</th>
<th>Relative Dispersal</th>
<th>Basis for Density Dependence</th>
<th>Breeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eggs</td>
<td>0</td>
<td>False</td>
<td>0</td>
</tr>
<tr>
<td>Cysts</td>
<td>0</td>
<td>True</td>
<td>0</td>
</tr>
<tr>
<td>Worms</td>
<td>1</td>
<td>False</td>
<td>1</td>
</tr>
</tbody>
</table>

Stage matrix

<table>
<thead>
<tr>
<th></th>
<th>Eggs</th>
<th>Cysts</th>
<th>Worms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eggs</td>
<td>0.0</td>
<td>0.0</td>
<td>600.0</td>
</tr>
<tr>
<td>Cysts</td>
<td>0.005</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Worms</td>
<td>0.0</td>
<td>1.0</td>
<td>0.1</td>
</tr>
</tbody>
</table>

Density dependence
Density dependence is Scramble, based on cyst abundance, and affects survival rates.

Catastrophe
Name: Dzhut (harsh winter)
Extent: Regional
Probability = 0.1
Affects abundances
Stage-specific multipliers:

<table>
<thead>
<tr>
<th>Eggs</th>
<th>Cysts</th>
<th>Worms</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>1.0</td>
<td>1.0</td>
</tr>
</tbody>
</table>

Dispersal
All migration/dispersal rates are symmetric (same in both directions).
Migration/dispersal rates (Mij) are based on the following function of the distance between populations (Dij):
Mij = 1.00 * exp(-Dij ^ 2.00 / 6.00), if Dij <= 100.00
Mij = 0.0, if Dij > 100.00
Dispersal depends on target pop. K
Table 3  Assumptions made in the modelling. Validity is the likelihood that the assumption holds for the particular system studied here.

<table>
<thead>
<tr>
<th>Assumptions</th>
<th>Explanation</th>
<th>Validity</th>
</tr>
</thead>
<tbody>
<tr>
<td>The parasite is in an endemic steady state</td>
<td>Parasite population size constant, insignificant effects of density-dependence, low reproductive ratio</td>
<td>Probably yes - Low prevalences, long-term parasite persistence</td>
</tr>
<tr>
<td>No acquired host immunity</td>
<td>Acquired immunity is the main density-dependent constraint, manifested as a non-linear host age-prevalence relationship</td>
<td>Probably yes - but no direct evidence. Rodents short-lived.</td>
</tr>
<tr>
<td>Rodent population sizes within patches relatively stable</td>
<td>If there is a strong predator-prey relationship between foxes and rodents then the relationships between dispersal, fecundity and carrying capacity will be too complex for the modelling framework</td>
<td>Probably yes - but inadequate data</td>
</tr>
<tr>
<td>Fox population sizes stable with foraging behaviour related simply to rodent density in patches and inter-patch distance</td>
<td>See above. Foxes are partially reliant on <em>R. opimus</em> at only one particular time of year. They are sedentary at this time, with relatively stable population sizes.</td>
<td>Probably yes - but inadequate data</td>
</tr>
<tr>
<td>Minimal parasite-related mortality or morbidity in either host</td>
<td>There is no feedback assumed between population size and habitat availability or transmission rate</td>
<td>Dubious for rodents - parasite can be found at high prevalence in foxes, but very low prevalence in rodents, which may suggest increased predation susceptibility of infected animals.</td>
</tr>
<tr>
<td>No significant loss of generality from annual rather than seasonal timestep</td>
<td>There are complex seasonal interactions between egg viability, host presence and foraging behaviour that we have not considered explicitly (they could be considered in RAMAS with better data availability)</td>
<td>Transmission is probably only significant at key points in the year (late spring)</td>
</tr>
<tr>
<td>Each host is a single species only</td>
<td>If multiple host species involved, complexity may increase enormously, particularly if they are biologically and behaviourally very different.</td>
<td>Field data suggest one intermediate and one definitive host in this particular area.</td>
</tr>
</tbody>
</table>
**Figure legends**

**Figure 1.** Simplified schematic representation of the lifecycle of *E. multilocularis*.

**Figure 2.** Main ecological zones of Kazakhstan, and prevalence of *E. multilocularis* as found in large-scale field studies carried out throughout the country (Shaikenov & Torgerson 2001). The areas discussed in this chapter are those where a low prevalence of *E. multilocularis* was found (hatched areas) in the desert region (pale dotted areas).

**Figure 3.** Output of the example model. In each case the mean is given as a solid line or bar, the error bars represent one standard deviation and the maximum value is given as a cross. The population is counted only as the number of cysts (excluding the eggs and adult worms). Results are from 50 iterations of 50 years duration. a) Abundance of cysts in the metapopulation as a whole; b) Number of occupied patches (excluding year 1, in which all 9 patches are occupied); c) Length of occupancy for each of the 9 patches.
Russia

China

Uzbekistan

Caspian Sea

Aral Sea

Lake Balkhash

Areas where *Echinococcus multilocularis* was found in the definitive &/or intermediate hosts at low prevalence (<1%)

Areas where *Echinococcus multilocularis* was found in the definitive &/or intermediate hosts at high prevalence (>1%)

Areas where definitive &/or intermediate hosts were examined but *Echinococcus multilocularis* was not found.