Fox tapeworm an underestimated threat - model for estimating risk of contact

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Abstract

The fox tapeworm *(Echinococcus multilocularis)* occurs across large areas of Europe, Asia and North America. In people it may cause the zoonotic infection, *alveolar Echinococcosis*. Incurable and fatal if not treated, it therefore requires costly, intensive, lifelong medication. To ensure efficient use of resources it is crucial to know where counter-measures are most beneficial. To assist prevention efforts, a model was developed based on prevalence rates in foxes (*Vulpes vulpes*), fox population densities, fox defecation rates and human population densities. The aim was to estimate and gain insight into the intensity of contamination in different environments and the relative probability of people coming in contact with tape worm eggs. Based on data from six Bavarian regions there was a strong positive correlation (Pearson r= + 0 .970, P≤0.001) between human cases of *alveolar Echinococcosis* and the relative probability of contact calculated by this model. Furthermore, the example calculations showed that due to the higher fox population density, just as much infectious material is released into the environment per day and per km^2 in urban areas with low prevalence (10%) as in rural areas with high prevalence (80%). If human population density is also taken into account, the likelihood of contact between people and infectious faeces is higher in suburban/urban than in rural areas. For example in 2005 the likelihood of contact was 45 times higher in the city of Munich than the Bavarian average. The model thus confirms the hypothesis of Deplazes et al (2004) , which emphasizes the substantial risk presented to humans by *Echinococcus multilocularis* in suburban areas, and calls for counter- measures.

Introduction

Across wide regions of Europe, with the exception of Great Britain (Smith et al. 2003), foxes (*Vulpes vulpes*) are infected with the fox tapeworm *Echinococcus multilocularis* (Eckert et al. 2001a, Romig et al. 2002). The prevalence rate (infection rate) of tapeworm infection in foxes varies according to regional conditions (Romig et al. 2002). Since the beginning of the 1990s fox populations in central Europe have increased three to four-fold (Breitenmoser-Würsten et al. 2001, Gloor et al. 2001, König et al. 2005). Foxes that originally inhabited forests and countryside have moved to cities and villages (Gloor et al. 2001, König 2005, König & Barla-Szabo 2005), as they did in the UK as early as the 1930s (Teagle 1967, Beames 1969).

Foxes living in close proximity to people may be carriers of the fox tapeworm (Hofer et al. 2000, Deplazes et al. 2002, König et al. 2005). In people, the tapeworm can cause a serious disease called *alveolar Echinococcosis*, a condition currently regarded as one of the most significant zoonoses in Europe (Pawlowski et al. 2001, Romig et al. 2002). It is incurable, necessitates lifelong medication and, if untreated, is fatal (Pawlowski et al. 2001, Romig et al. 2002). As there is a correlation between fox population density and incidence of the disease in humans (Notdurft et al. 1996, Schweiger et al. 2007, König et al. 2008), an increase in *alveolar Echinococcosis* (AE) is to be expected in suburban areas after foxes have settled there (Deplazes et al. 2004). Because of the seriousness of the disease and the enormous costs involved, measures are required at the state, county and municipal levels to reduce the risk of human infection (Ito et al. 2003). As there is currently no effective cure for humans, the risk of infection can only be reduced by preventative measures with a primary focus on minimizing environmental conditions favouring the accumulation of infectious material (Beaglehole et al. 1997). Although education programs can help to reduce the risk of infection for the human population, they are often time-consuming, labor-intensive, and ineffective in reaching all sectors of the population (Eckert et al. 2001b). The fox hunting advocated mainly by hunting associations has failed in attempts to reduce rabies (Macdonald 1980, Anderson et al. 1981, Romig et al. 2007). Due to hunting regulations, it is not allowed anyway in suburban/urban areas (Leonhardt 1986). The only effective measure left is therefore to treat foxes with the anthelminitic praziquantel. This drug kills the parasite in the host organism (Andrews et al. 1983) and, in turn, reduces the amount of infectious material in the environment (Hegglin et al. 2003, Romig et al. 2007, König et al. 2008), thereby minimising the infection risk for humans.

Although the costs of a praziquantel treatment program are estimated at 1.00 € to 3.00 € per head, the efficiency and necessity of this approach must be carefully assessed (Siebert 2006). At present the current regional or local human infection risk in Germany cannot be given, because the availability of statistics is restricted to areas of larger scale. The current incidence of *alveolar Echinococcosis* does not reflect the current infection risk anyway, because in general 15 years pass between infection and the appearance of symptoms (Schweiger et al. 2007). During this time, however, not only have foxes moved into suburban / urban areas, but the prevalence rates among foxes have also increased. If statements are to be made about the current infection risk for people, it must be described in terms of exposure (Romig et al. 2002).

One way of assessing exposure risk is to examine the prevalence rates in foxes (Romig et al. 2002), which are known to be highest in agricultural (Viel et al. 1999, Giraudoux et al. 2002, Weible 2005) and lowest in suburban / urban areas (Deplazes et al. 2004, König et al. 2005). It is also necessary to take into account the fox population density which, depending on the season, varies between 0.7 and over 30 foxes / km² (Harris

1981, Labhardt 1996, König 2005). In a very general approach, Deplazes et al. (2004) hypothesized that the risk of catching *alveolar Echinococcosis* increases in recreational and suburban areas (i.e. areas with detached / semi-detached houses and surrounding gardens). However, his hypothesis is too indefinite to help in the decision-making process. Epidemiological decision processes are all too often based on cost-benefit analyses (Siebert 2006). The prerequisites for these are quantifiable parameters or risks.

Our objective in this study was to develop a model to quantify the current risk to people of catching *alveolar Echinococcosis*. To move forward, so-called, “reference areas” were defined (state of Bavaria or the Federal Republic of Germany).The regional or local contact likelihood was calculated relative to the average risk within the reference area. This resulted in a quantifiably higher or lower contact likelihood relative to the reference area.

Using this model, the distribution of praziquantel can be optimised to maximize the efficiency of the use of financial resources.

Material and methods

To calculate the likelihood of contact between humans and fox tapeworm eggs as a measure of infection risk, the following factors were included in the model: fox population density, prevalence or prevalence rate (i.e infection rate) in foxes, infection intensity or worm burden, and human population density.

Fox population density

Data on population density and on annual population increment were taken from published literature:

Spring:

- 0.7-2 foxes / km² in agricultural (forest and farmland) and recreational areas in Germany (Vos 1993, Labhardt 1996, Stiebling 2000).
- 5-8 foxes / km² in villages and towns with fewer than 10 000 inhabitants (Janko et al. 2007),
- 6 – 20 foxes / km², an average of 10-12 adult foxes / km^2 in urban and suburban areas (Harris 1981, Hegglin et al. 2003, König 2005).

An average annual increment of 4-5 pups / fox territory (Harris 1979, Harris 1981, Marks & Bloomfield 1999) would suggest that the summer density rises to approximately 2-7 foxes/km² (Stubbe 1986, Funk & Gürtler 1990, Stiebling 2000) in agricultural areas, and to approximately 14-32 foxes / km^{2}in suburban and urban areas.

Diagnosis of infection with fox tapeworm Echinococcus multilocularis

The diagnosis was made by Romig at the University of Hohenheim by taking smears from foxes harvested during the hunting period by amateur hunters in areas where tapeworm risk analysis projects were being carried out (compare also König et al. 2005, 2008). The research group asked for the carcasses in order to find out the prevalence rate.

For this the animals were dissected and swabs were then taken of the mucosa of the small intestine (intestinal scraping technique - ITS) (Eckert et al. 2001c). This tried, tested and time-saving method allows the presence of the fox tape worm to be proven directly under the microscope. Once coarse parts of the contents of the small intestine are removed, 15 swabs are taken from the mucosa and put on to glass slides. These are then placed in square petri-dishes (9 x 9cm) and examined under the binocular microscope, which magnifies them by a factor of twelve. This allows a 100% specific diagnosis, a semi-quantitative assessment of the degree of prevalence. In addition it establishes the development stage of the parasites (patent-prepatent). Compared with the time-consuming sedimentation method (“gold standard”), a sensitivity of 78% is given (Hofer et al. 2000).

Prevalence rate in foxes in Bavaria and study areas

The average prevalence rate in foxes in the state of Bavaria (south Germany) was roughly 33% in 2006 (Bavarian State Institute for Public Health 2007). The values reported for Bavaria by the Bavarian State Institute for Public Health represent an average of the results of investigations carried out between 1988 and 2006. In order to develop our model, it was necessary to explore the prevalence rate and focus on a mixture of larger and smaller communities and rural areas (the Starnberg region with the town of Starnberg and a lot of villages, the city of Munich, the villages of Oberammergau and Utting and, in the Isar valley, the villages of Baierbrunn, Icking, Pullach, Schäftlarn).

Infection intensity or worm burden

In order to demonstrate a possible correlation between prevalence rates in foxes and infection intensities (worm burden), the prevalence rates and infection intensities recorded in the risk analysis projects in Starnberg county (König et al. 2005), the villages of Oberammergau and Utting, and the Isar valley were compared. As prevalence of less than 25% was rare in these studies, data for the city of Munich was requested from the Bavarian State Institute for Public Health and included in the analysis. This data categorised the infection intensity into classes, so it was necessary to apply these to our own data. The following infection intensity classes were established according to the number of tapeworms found:

0, <10, 10-19, 20-49, 50-99, 100-499, 500-999, >999 (eggs).

In addition the prevalence rate was divided into the following classes according to Weible (2005): 0, <30, 30-60,>60 (%).

In general, only positive sections from foxes were included. Data from areas where worming programmes had already started were not considered. It cannot be ruled out that the worming programme not only reduces the prevalence rate but also the worm burden.

Daily defecation rate of foxes

Webbon et al. (2004) recorded an average defecation rate of 8 lots of faeces per fox and day. This value was also applied in our study.

Model

The model quantifies the differences between the general likelihood of contact for people in a reference area and the likelihood for people in the area of interest. To do this any area can be chosen. In the example given Bavaria was selected as the reference area. The model then shows whether there is a higher or lower likelihood of contact for inhabitants of the area of interest in relation to the reference area, given their specific mode of behaviour and habits. The area of interest can be a region, a state, but also a localised, smaller geographical unit. If the same reference area is used for several analyses, several areas of interest can be compared directly with regard to the likelihood of infection for people.

The first step in measuring risk of contact is to calculate the amount of infectious faeces/ km^2 from the fox population density and prevalence rates. Secondly, as the likelihood of humans coming in contact with the infectious faeces also depends on human population density, infectious faeces/ km^2 are weighed against the number of inhabitants per km^2.

So the average contact likelihood for Bavaria is calculated from three parameters: average fox population density, prevalence rate in foxes and human population density. This result for Bavaria is taken as the reference and is set at 1. This method of calculation is also applied for the area of interest. If there is a higher or lower likelihood of infection in the area of interest, this is then illustrated in relation to the reference area.

$$\text{Infection likelihood}_{\text{Target / Reference}} = \frac{\text{fox density}_{\text{Target}} * \text{prevalence}_{\text{Target}} * \text{human population density}_{\text{Target}}}{\text{fox density}_{\text{Reference}} * \text{prevalence}_{\text{Reference}} * \text{human population density}_{\text{Reference}}}$$

General mathematical term of the model:

T = Target =area of interest (e.g. Munich, Oberammergau, or Upper Bavaria)

B=Basis= reference area (e.g. Bavaria, Germany, or Europe)

R=infection likelihood (for an area relative to a reference area)

D=fox density

P=prevalence rate in foxes

H=human population density

$$R_{T/B} = \frac{D_T * P_T * H_T}{D_B * P_B * H_B}$$

DR (= average defecation rate of foxes) is a constant in both numerator and denominator of the formula and can therefore be left out.

Statistical methods

The correlation between prevalence rate and infection intensity classes was assessed by using Spearman Rho, with $P<0.05$ being considered significant.

To evaluate the model, the correlation between the incidence of *alveolar Echinococcosis* in the six Bavarian regions and the regional likelihood *alveolar Echinococcosis* calculated by the model was assessed, using Pearson r, with $P<0.05$ being considered significant.

The increase in prevalence rates in foxes in Munich and the comparison of the prevalence rates in foxes within and outside the community of Oberammergau were tested using the Mann-Whitney U test, with $P<0.05$ being considered significant.

Results

Prevalence of tapeworm infection in foxes in different areas

Table 1 presents the prevalence rates of tapeworm infection in foxes in different communities and Table 2 shows the prevalence rate in foxes in rural areas in Upper Bavaria. Prevalence rates vary between 15 % and 80%. What is striking here is a significant increase in prevalence rates within the city of Munich (Table 1) from 13 % in 2002, to 25% in 2005 (Mann-Whitney U $P \leq 0.001$) . Furthermore there is no significant difference between the prevalence of tapeworm in foxes within (40%) (Table 1) and outside (36%) (Table 2) the community of Oberammergau (Mann-Whitney U $P=0.102$). The prevalence of fox tapeworm in foxes in communities of more than 10,000 inhabitants with urban fox populations (suburban areas of Munich, Krailling, Planegg, Neuried) is lower than the prevalence rate in rural areas or small villages with rural fox populations.

Worm burden in foxes in relation to average prevalence in a fox population

To establish a correlation between prevalence rate and infection intensity, the frequency of the infection intensity classes are presented in Table 3 in relation to prevalence rate classes. According to this data no correlation was traced between worm burden in foxes and the mean prevalence of fox tapeworm in fox populations (Rho=0.019, p= 0.732). The average values for infection intensity are between 20 and 49 worms per fox. As there is no correlation according to the data presented, no further account is taken of this in the construction of the model.

Figure 1 shows the numerical relation between fox population density, prevalence rate in foxes, and infectious faeces per day and km². Given a fox population density of 1 fox per km^2 in a rural area and a prevalence rate of 80%, approx. 6 infectious lots of faeces contaminate the environment every day. The quantity is the same with 4 foxes per km^2 and a prevalence rate of 20%, or 8 foxes and a prevalence rate of 10%, e.g. in suburban areas.

Model validation

In order to get a reference for the infection likelihood for people, an average value was derived from a Bavarian mean prevalence rate of 33% in foxes and a mean Bavarian winter fox population density of 2 foxes per km^2.

If we then also take into account the human population density of 176 inhabitants per km^2 in Bavaria (Bavarian Government 2010), the outcome is a dimensionless value for the whole of Bavaria as reference area, which as a reference = 1.

To validate the described model, Table 4 shows the prevalence rates in foxes and the number of humans with *alveolar Echinococcosis* in the six Bavarian regions. If we calculate the likelihood of contact for the different regions by applying the model described above, the relative likelihood of people coming in contact with the fox tapeworm is 161% of the Bavarian average in Swabia, and 149% in Upper Bavaria (Table 4). The lowest likelihood of contact is in Lower Bavaria, at just 23% of the Bavarian average. It shows a very close, positive correlation (Pearson r= + 0 .970, P<0.000) between *alveolar Echinococcosis* and the relative likelihood of contact. The coefficient of determination (B) is 0.94, i.e. 94% of the cases can be explained using the model.

Below are examples to demonstrate how the model is applied.

Supposing the whole of Bavaria is used as a reference area and data from the district of Starnberg is entered in the model (fox population density of approx. 2 per km^2, 266 residents per km^2 (Bavarian Government 2010) and 55 % prevalence in foxes (König et al. 2005)), it demonstrates a likelihood of contact between Starnberg inhabitants and fox tapeworm eggs of 250 % above the Bavarian average. If we take the community of Oberammergau (c.f. Table 2), the likelihood rises to as high as 299 %, and finally, in the community of Herrsching (c.f. Table 2), district of Starnberg, it amounts to 1,636 % of to the Bavarian average.

If we look at the suburban area of Munich, with between 2,100 and 5,448 residents per km^2 (Lang & Wiegandt 2003), the likelihood of contact taking place between humans and infectious eggs in 2002 (prevalence rate 13%) was at least 23 times or 2,330 % of the Bavarian average (given 2,100 inhabitants per km^2 in suburban areas). Only three years later, in 2005, (prevalence rate 25%) it had increased to 4,481 %.

These calculations can be carried out for any area and at random.

Discussion

The model presented here for calculating the likelihood of contact between people and fox tapeworm eggs allows us to quantify the risk of human infection with *alveolar Echinococcosis.* This is done by looking at the general likelihood of contact relative to a reference area, whereby the area of interest can be either small or large. Using the data available for Bavaria on *alveolar Echinococcosis* in humans, there is a close correlation ($r=0.970$, $P<0.000$) between the prediction given by the model and the actual incidence.

As such the model provides an important base for epidemiological decision-making processes (Siebert 2006). Above all it is the key to a cost-benefit analysis for minimizing the risk of *alveolar Echinococcosis.* If the same reference area is taken, the different general likelihood of contact and thus the infection risks in different areas can be compared. The accuracy of the prediction always depends on the quality of the data it is based on, however. Consequently, the calculations carried out in the model demonstrated agreement with the thesis of Deplazes et al.(2004), stating that it is in the suburban areas (such as villages or suburban areas in towns and cities) in particular that there is an alarming increase in *alveolar Echinococcosis*. For example the model shows that in Munich, with a prevalence rate of 25% in foxes, the likelihood of contact and thus the risk of infection for its population is 45 times higher than the Bavarian average. Despite this low prevalence rate in foxes, it is a human health issue of considerable concern. According to Rehkugler and Schindel (1990), however, for a general estimation of risk, it is irrelevant to consider the behaviour of any human individual. Having said that, people who spend a lot of time in the garden or keep pets run a higher risk than those who don’t (Kern et al. 2004).

For estimating the individual risk of infection, it was possible to show in Figure 1 that, contrary to common perceptions, there are in fact more infectious fox faeces per km² in suburban areas than in forests and fields. Despite lower prevalence rates in foxes, not only the risk to the population as a whole, but also the risk to individuals of contracting *alveolar Echinococcosis* is thus highest in suburban areas. This also means that in suburban areas, not only is the likelihood of humans generally coming in contact with tapeworm eggs higher, due to the human population density, but the individual infection risk is also higher, since there are greater amounts of infectious faeces due to a bigger fox population. This problem not only exists in the suburbs of a city - it may also occur in inner-city areas.

Input data for the model are prevalence rates in foxes, fox population densities and number of inhabitants. The “defecation rate” is a constant in both numerator and denominator of the formula and can thus be left out. The infection intensity (worm burden) did not result in further differentiation.

Other factors influencing the survival of tapeworm eggs, such as the nature of the surface (grass), precipitation, or temperature development (Giraudoux et al. 2002) were not included in the model calculation. These parameters effect the tapeworm eggs’ survival chances on the soil (Giraudoux et al. 2002), and were indirectly considered via local prevalence rates in foxes. As the silvatic cycle of foxes causing contamination of the soil with eggs is predominant in both towns and the countryside, the role of cats and dogs was ignored (Eckert und Deplazes 1999, Eckert et al. 2001a, Deplazes, et al. 2002, Giraudoux et al. 2002, Romig et al. 2002). Greater differentiation within rural areas, such as between forest, meadows, arable land, or mixed forms, as stated by Weible (2005), would be possible in the model by using the specific fox population densities or prevalence rates among foxes.

In contrast to the findings of Weible (2005), no link between infection intensity (worm burden) and prevalence rate in foxes could be established in the investigations carried out in southern Bavaria. This result tallies with that of Immelt (2007), who was also unable to establish a link on the basis of data from Hessen (Germany). The deviating results of Weible (2005) could possibly derive from the circumstance that some of the data was from areas in which foxes were treated with anthelmintics. We had similar results in our anthelmintic treatment areas.

The data on prevalence rates in foxes used as a basis for the model calculations are taken from real recordings. According to the categories of Weible (2005), the prevalence rate of 25% in foxes in Munich (table 1) is classed as “slight infestation”. As illustrated in Figure 1, the infectious material contained in faeces in Munich exceeds the quantity released in a rural area with “high infestation” according to Weible (2005). This shows that for infection assessment, the prevalence rate in foxes alone does not tell us much.

However, prevalence rates in foxes, fox population densities and human population development can be integrated in the model to estimate and quantify future developments in infection risks. It is this possibility of being able to combine real figures with data from literature that allows flexible and universal application of the model in the decision-making processes.

It is known that the time span between infection and the appearance of the first symptoms of *alveolare Echinococcosis* is 15 years (Schweiger et al. 2007). It is therefore evident that the model represents an important instrument for forward-looking health care and an appropriate response to the threat posed by the fox tapeworm.

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Table 1: Prevalence rates in suburban and urban areas (CI according to Cannon & Roe 1990)

Community	Time period	Preva-lence rate	N	CI (95%)	Source
Munich *	2002	13%	61	6% - 25%	Kopp 2007
Munich*	2003	21%	47	10% - 35%	Kopp 2007
Munich*	2004	21%	63	11% - 34%	Kopp 2007
Munich*	2005	25%	81	16% - 36%	Kopp 2007
Krailling, Planegg, Neuried*	2002 / 2003	15%	26	4-45	König et al. 2005
Oberammergau	2002-2004	40%	45	31%-61%	pers. data

*Community with more than 10.000 inhabitants

Table 2: Prevalence rates mainly in rural areas (CI according Cannon & Roe 1990)

Community	Time period	Prevalence of infection	No. of foxes examined	CI (95%)	Source
Utting	2003	47%	56	33%-61%	pers. data
Isartal	2005	35%	58	22%-49%	pers. data
Andechs, Gilching, Herrsching, Inning, Weßling, Wörthsee	02 / 03	80 %	82	70%-88%	König et al. 2005
Berg, Tutzing Feldafing, Starnberg, Pöcking, Gauting	02 / 03	47 %	119	38%-57%	König et al. 2005
Oberammergau	02-04	36%	22	20%-55%	pers. data

Table 3: Prevalence rates and infection intensity (according to Weible 2005)

	Infection intensity (Worm-burden) class							
Prevalence class	<10	10-19,	20-49,	50-99,	100-499,	500-999,	>999	N
1-29%	23.5%	20.0%	16.5%	16.5%	12.9%	7.1%	3.5%	85
30-60%	27.4%	9.1%	17.7%	16.0%	17.7%	5.1%	6.9%	175
>60%	27.3%	7.8%	24.7%	6.5%	29.9%	2.6%	1.3%	77
Total	26.4%	11.6%	19.0%	13.9%	19.3%	5.0%	4.7%	337

Table 4: Prevalence rates of fox tapeworm infection in foxes in Bavaria (Nothdurft et al. 1996), human AE cases (RKI 2010, Nothdurft et al 1996) and likelihood of contact of humans with fox faeces

Area	Positive foxes (%)	Human cases (N)	Likelihood of contact of humans with fox faeces
Bavaria (all)	33 %	101	100 %
Swabia	44 %	48	161 %
Upper Bavaria	33 %	32	149 %
Lower Bavaria	13 %	4	23 %
Upper Palatinate	16 %	5	29 %
Upper Franconia	21 %	6	55 %
Middle Franconia	8 %	5	32 %
Lower Franconia	13 %	1	31 %

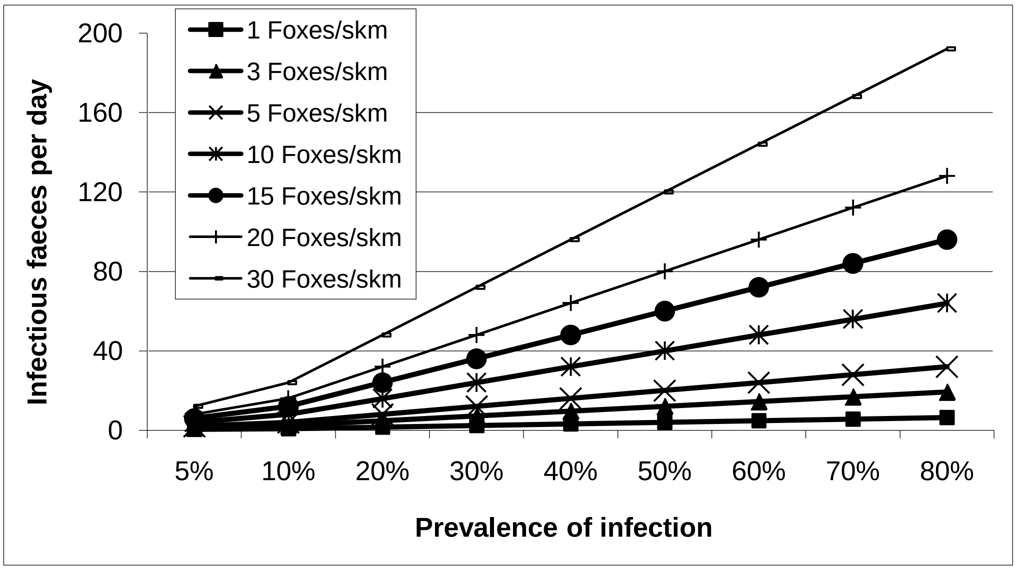

Figure 1: Fox population density, prevalence rates and infectious faeces per km²