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Authors: König, Andreas, and Romig, Thomas

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Original article

Fox tapeworm *Echinococcus multilocularis*, an underestimated threat: a model for estimating risk of contact

Andreas König & Thomas Romig

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 (AE). Incurable and fatal if left untreated, it therefore requires costly, intensive and lifelong medication. To ensure efficient use of resources it is crucial to know where counter-measures are most beneficial. To assist prevention efforts, we developed a model based on prevalence rates in red foxes *Vulpes vulpes*, fox population densities, fox defecation rates and human population densities. Our aim was to estimate and gain insight into the intensity of contamination in different environments and the relative probability of people coming into contact with tape worm eggs. Based on data from six Bavarian regions, there was a strong positive correlation (Pearson $r = +\ 0.970$, $P \leq 0.001$) between human cases of AE and the relative probability of contact calculated using 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 of fox tapeworms (10%) as is 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. Our model thus confirms the hypothesis of Deplazes et al. (2004), which emphasises the substantial risk presented to humans by fox tapeworms in suburban areas, and it calls for counter-measures.

Key words: Human-wildlife conflict management, urban wildlife, Vulpes vulpes, wildlife diseases, zoonosis

Andreas König, Wildlife Biology and Management Unit, Chair of Animal Ecology, Technische Universität München, Am Hochanger 13, D-85354 Freising, Germany - e-mail: koenig@wzw.tum.de
Thomas Romig, Parasitology Department, University of Hohenheim, Emil-Wolff-Strasse 34, D-70599 Stuttgart, Germany - e-mail: romig@uni-hohenheim.de

Corresponding author: Andreas König

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Across wide regions of Europe, with the exception of Great Britain (Smith et al. 2003), red foxes *Vulpes vulpes* are infected with the fox tapeworm *Echinococcus multilocularis* (Eckert et al. 2001c, 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 spread to cities and villages (Gloor et al. 2001, König 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 (AE), 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 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 minimising environmental conditions favouring the accumulation of infectious material (Beagleholde et al. 1997). Although education programmes can help to reduce the risk of infection for the human population, they are often time-consuming, labour-intensive and ineffective in reaching all sectors of the population (Eckert et al. 2001b). Fox hunting advocated mainly by hunting associations has failed in attempting to reduce rabies (Macdonald 1980, Anderson et al. 1981, Romig et al. 2007). Nevertheless, due to hunting regulations, fox hunting is not allowed anywhere in suburban/urban areas (Leonhardt 1986). Therefore, the only effective measure left is 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 programme are estimated at 1.00-3.00 € per head and year, 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 as the availability of statistics is restricted to areas of larger scale. The current incidence of AE does not reflect the current infection risk anyway, because in general 15 years pass between the infection and the appearance of symptoms (Schweiger et al. 2007). During this time, however, foxes have not only 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 > 30 foxes/km^2 (Harris 1981, Labhardt 1996, König 2005). In a very general approach, Deplazes et al. (2004) hypothesised that the risk of catching AE increases in recreational and suburban areas (i.e. areas with detached/semi-detached houses and surrounding gardens). However, their 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 the decision processes are quantifiable parameters or risks.

The objective of our study was to develop a model to quantify the current risk to people of catching AE. To move forward, we defined 'reference areas', i.e. state of Bavaria or the Federal Republic of Germany. We calculated the regional or local contact likelihood 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 maximise 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

We used data on population density in spring and on annual population increment for the following types of areas:

- Agricultural (forest and farmland) and recreational areas in Germany: 0.7-2 foxes/km^2 (Vos 1993, Labhardt 1996, Stiebling 2000).
- Villages and towns with $< 10{,}000$ inhabitants: 5-8 foxes/km^2 (Janko et al. 2007),
- Urban and suburban areas: 6-20 foxes/km^2 with an average of 10-12 adult foxes/km^2 (Harris 1981, Hegglin et al. 2003, König 2005).

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

Diagnosis of infection with fox tapeworm

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

For this purpose we dissected the animals and then took swabs of the mucosa of the small intestine (intestinal scraping technique, ITS; Eckert et al. 2001a). This tried, well-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 had been removed, we took 15 swabs from the mucosa and put it on glass slides, which were then placed in square petri-dishes of 9 × 9 cm and examined under the binocular microscope (x 12) leading to a 100% specific diagnosis; a semi-quantitative assessment of the degree of prevalence. It also made it possible to establish the developmental stage of the parasites (patent or prepatent). Compared with the time-consuming sedimentation method ('gold standard'), a sensitivity of 78% has been obtained by Hofer et al. (2000).

Prevalence rate in foxes in Bavaria and the study areas

The average prevalence rate in foxes in the state of Bavaria (i.e. 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 many villages, the city of Munich, the villages of Oberammergau and Utting, the Isar valley, and the villages of Baierbrunn, Icking, Pullach and 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 the county of Starnberg (König et al. 2005), the villages of Oberammergau and Utting, and the Isar valley were compared. As prevalence of $< 25\%$ was rare in these studies, we requested data for the city of Munich from the Bavarian State Institute for Public Health and included these data in the analysis. The data categorised the infection intensity into classes, therefore it was necessary to apply these classes to our own data. According to the number of tapeworm eggs found, we established the following eight infection intensity classes: 0, < 10, 10-19, 20-49, 50-99, 100-499, 500-999, > 999. In addition, we divided the prevalence rate (in %) into the following four classes according to Weible (2005): 0, < 30, 30-60, > 60.

In general, we included only positive sections from foxes. Data from areas in which worming programmes had already been initiated, were not considered. We cannot rule 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 eight lots of faeces/fox/day. We also applied this value in our study.

Model

Our 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 or 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 the risk of contact was to calculate the amount of infectious faeces/km^2 from the fox population density and prevalence rates. Secondly, as the likelihood of humans coming into contact with the infectious faeces also depends

Table 1. Prevalence rates in red foxes in suburban and urban areas. The CI 95% are according to Cannon & Roe (1990).

Community	Time period	Prevalence 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%	Our data

* Community with > 10,000 inhabitants.

on the human population density, infectious faeces/km^2 were weighed against the number of inhabitants/km^2.

Accordingly, the average contact likelihood for Bavaria was calculated from three parameters: average fox population density, prevalence rate in foxes and human population density. We took this result for Bavaria as the reference and set it equal to 1. This method of calculation was also applied for the area of interest. If there was a higher or lower likelihood of infection in the area of interest, this was then illustrated in relation to the reference area in the following way:

$$\text{Infection likelihood}_{\text{Target/Reference}} = (\text{fox density}_{\text{Target}} * \text{prevalence}_{\text{Target}} * \text{human population density}_{\text{Target}}) \div (\text{fox density}_{\text{Reference}} * \text{prevalence}_{\text{Reference}} * \text{human population density}_{\text{Reference}}).$$

The general mathematical term of the model was: 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 and

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

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

Statistical methods

We assessed the correlation between prevalence rate and infection intensity classes by use of Spearman Rho with $P < 0.05$ being considered significant.

To evaluate the model, we assessed the correlation between the incidence of AE in the six Bavarian regions and the regional likelihood of AE calculated by the model by use of Pearson r with $P < 0.05$ being considered significant.

We tested 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 using the Mann-Whitney U-test, with $P < 0.05$ being considered significant.

Results

Prevalence of tapeworm infection in foxes in different areas

The prevalence rates of tapeworm infection in foxes in different communities and the prevalence rate in foxes in rural areas in Upper Bavaria are shown in Tables 1 and 2, respectively. The prevalence rates varied between 15 and 80%. The significant increase in prevalence rates within the city of Munich is

Table 2. Prevalence rates in red foxes mainly in rural areas. The CI 95% are according to Cannon & Roe (1990).

Community	Time period	Prevalence of infection	No. of foxes examined	CI (95%)	Source
Utting	2003	47%	56	33 - 61%	Our data
Isartal	2005	35%	58	22 - 49%	Our data
Andechs, Gilching, Herrsching, Inning, Weßling, Wörthsee	2002/2003	80%	82	70 - 88%	König et al. 2005
Berg, Tutzing Feldafing, Starnberg, Pöcking, Gauting	2002/2003	47%	119	38 - 57%	König et al. 2005
Oberammergau	2002/2004	36%	22	20 - 55%	Our data

Table 3. Prevalence rates in red foxes 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

striking (see Table 1); from 13 in 2002 to 25% in 2005 (Mann-Whitney U-test: $P \leq 0.001$). Furthermore there was no significant difference between the prevalence of tapeworm in foxes within (40%; see Table 1) and outside (36%; see Table 2) the community of Oberammergau (Mann-Whitney U-test: $P = 0.102$). The prevalence of fox tapeworm in foxes in communities with >10,000 inhabitants and in urban fox populations (i.e. the suburban areas of Munich, Krailling, Planegg and Neuried) was 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, we present the frequency of the infection intensity classes in Table 3 in relation to the prevalence rate classes. We traced, according to the data in Table 3, no correlation 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 were between 20 and 49 worms per fox. As there was no correlation according to the data presented, no further account was taken of this in our construction of the model.

The numerical relation between fox population density, prevalence rate in foxes and infectious faeces/day/km^2 are shown in Figure 1. Given a fox population density of 1 fox/km^2 in a rural area, a prevalence rate of 80% and approximately only every second tapeworm is at the same time infectious, about three infectious lots of faeces contaminate the environment every day. The quantity is the same with 4 foxes/km^2 and a prevalence rate of 20%, or eight 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, we derived an average value from a Bavarian mean prevalence rate of 33% in foxes and a mean Bavarian winter fox population density of 2 foxes/km^2.

If we then also take into account the human population density of 176 inhabitants/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 is = 1.

To validate the described model, the prevalence

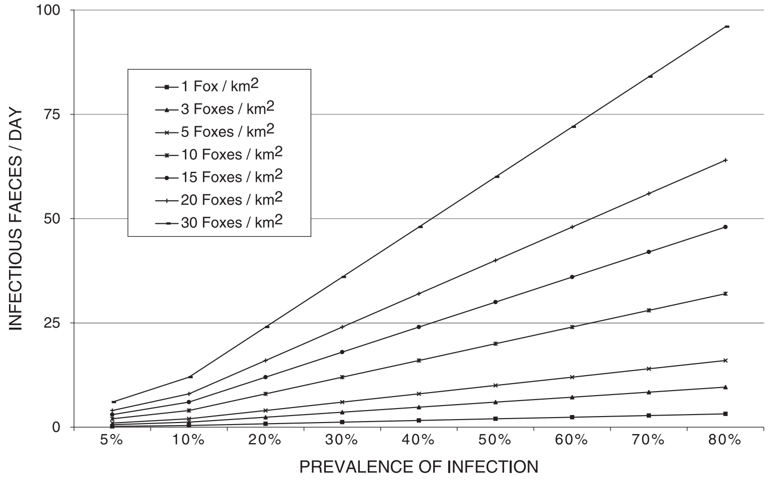

Figure 1. Fox population density, prevalence rates and infectious faeces/km^2.

Table 4. Prevalence rates of fox tapeworm infection in red foxes in Bavaria (based on Nothdurft et al. 1996), human AE cases (Robert Koch-Institut 2010, Nothdurft et al. 1996) and likelihood of contact of humans with fox faeces.

Area	Positive foxes (%)	Human cases (N)	Likelihood of human contact 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%

rates in foxes and the number of humans with AE in the six Bavarian regions are shown in Table 4. 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 (see Table 4). The lowest likelihood of contact was in Lower Bavaria, i.e. at just 23% of the Bavarian average. It shows a very close, positive correlation (Pearson's $r = + 0.970$, $P < 0.000$) between AE and the relative likelihood of contact. The coefficient of determination (B) was 0.94, i.e. 94% of the cases can be explained using the model.

In the following we present examples to demonstrate how the model is applied. Supposing that the whole of Bavaria is used as a reference area and data from the district of Starnberg are entered into the model (a fox population density of approximately 2/km^2, 266 residents/km^2 (Bavarian Government 2010) and 55% prevalence in foxes; König et al. 2005), it establishes a likelihood of contact between the inhabitants of Starnberg and fox tapeworm eggs of 250% above the Bavarian average. In, for instance, the community of Oberammergau (see Table 2) the likelihood rises to as much as 299%, and finally, in the community of Herrsching (see Table 2), the district of Starnberg, it increases to 1,636% of the Bavarian average.

Concerning the suburban area of Munich, which is comprised of 2,100-5,448 residents/km^2 (Lang & Wiegandt 2003), the likelihood of contact taking place between humans and infectious eggs in 2002 (with a prevalence rate of 13%) was at least 23 times or 2,330% of the Bavarian average (based on 2,100 inhabitants/km^2 in suburban areas). Only three years later, i.e. in 2005, (with a prevalence rate 25%) the likelihood had increased to 4,481%.

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

Discussion

The model we present here for calculating the likelihood of contact between people and fox tapeworm eggs allows us to quantify the risk of human infection with AE. We do this 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 AE in humans, there is a close correlation between the prediction given by the model and the actual incidence ($r = 0.970$, $P < 0.000$).

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 minimising the risk of AE. If the same reference area is taken, the different general likelihood of contact and thus the infection risks in different areas can be compared. However, the accuracy of the prediction always depends on the quality of the data it is based upon. Consequently, the calculations we 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 AE. 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 & 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 frequent amount of time in the garden or keep pets run a higher risk than those who do not (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/km^2 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 AE 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, but may also occur within metropolitan areas as well.

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 that influence the survival of tapeworm eggs, such as the nature of the surface (grass), precipitation or temperature development (Giraudoux et al. 2002), we did not include in the model calculation. These parameters affect the tapeworm eggs' survival chances in 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 in the countryside, we ignored the role of cats *Felis catus* and dogs *Canis familiaris* (Eckert & Deplazes 1999, Eckert et al. 2001c, 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 and could be obtained 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 (i.e. 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 obtained by Weible (2005) may derive from the circumstance that part of her data was from areas in which foxes were treated with anthelmintics. We obtained similar results in our anthelmintic treatment areas.

We took the data on prevalence rates in foxes used as a basis for the model calculations from real recordings. According to the categories of Weible (2005), the prevalence rate of 25% in foxes in Munich (see Table 1) is classified as a '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 the possibility of being able to combine real figures with data from the literature that allows flexible and universal application of the model in the decision-making processes.

It is well-known that the time span between infection and the appearance of the first symptoms of AE 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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