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A Quantitative Release Assessment for the Noncommercial Movement of Companion Animals: Risk of Rabies Reintroduction to the United Kingdom

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In 2004, the European Union (EU) implemented a pet movement policy (referred to here as the EUPMP) under EU regulation 998/2003. The United Kingdom (UK) was granted a temporary derogation from the policy until December 2011 and instead has in place its own Pet Movement Policy (Pet Travel Scheme (PETS)). A quantitative risk assessment (QRA) was developed to estimate the risk of rabies introduction to the UK under both schemes to quantify any change in the risk of rabies introduction should the UK harmonize with the EU policy. Assuming 100% compliance with the regulations, moving to the EUPMP was predicted to increase the annual risk of rabies introduction to the UK by approximately 60-fold, from 7.79×10^{-5} (5.90×10^{-5}, 1.06×10^{-4}) under the current scheme to 4.79×10^{-3} (4.05×10^{-3}, 5.65×10^{-3}) under the EUPMP. This corresponds to a decrease from 13,272 (9,408, 16,940) to 211 (177, 247) years between rabies introductions. The risks associated with both the schemes were predicted to increase when less than 100% compliance was assumed, with the current scheme of PETS and quarantine being shown to be particularly sensitive to noncompliance. The results of this risk assessment, along with other evidence, formed a scientific evidence base to inform policy decision with respect to companion animal movement.

KEY WORDS: Companion animals; rabies; risk assessment; UK

1. INTRODUCTION

Rabies is a zoonotic viral disease that causes acute encephalitis in humans and other warm-blooded animals; the clinical disease is untreatable and almost always fatal. Transmission occurs usually through saliva via the bite of an infected animal, with dogs being the main transmitter of rabies virus to humans. The United Kingdom (UK) is officially classified as being free from terrestrial rabies;(1,2) the last case of indigenous terrestrial animal rabies was in 1922. This rabies-free status was historically achieved by the investigation of every case of suspected disease and strict controls on dog and cat movements, and then maintained by the enforcement of a six-month quarantine period for all animals entering from abroad.

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Table I. A Comparison of the Requirements of the Various Pet Movement Policies Considered in this Risk Assessment; Six-Month Quarantine in the United Kingdom (UK), the UK Pet Travel Scheme (PETS), and the European Union Pet Movement Policy (EUPMP) for EU Members States and Listed Countries ($EUPMP_{EU\&listed}$) and Unlisted Countries ($EUPMP_{unlisted}$)

Requirement	Movement Policy			
	Quarantine	PETS	$EUPMP_{EU\&listed}$	$EUPMP_{unlisted}$
Microchip	No	Yes	Yes	Yes
Vaccination	Yes (once in UK)	Yes	Yes	Yes
Blood sample	No	Yes	No	Yes
Waiting period	6 months (in UK quarantine)	6 months	21 days	3 months

The current UK scheme for the movement of companion animals (dogs, cats, and ferrets), the Pet Travel Scheme (PETS), has been in place since 2000. This scheme allows companion animals from European Union (EU) Member States (MSs) and equivalents, and listed third countries, to enter the UK via a process involving microchipping for identification, vaccination against rabies, and serological testing for rabies-specific antibodies. After successful testing the animal must complete a six-month waiting period and receive tick and tapeworm treatment 24–48 hours before entry into the UK.[3] Companion animal entries from countries that do not qualify for PETS must complete six months in quarantine at a UK quarantine center, during which time the animal is vaccinated against rabies. Before 2000, all companion animal entries to the UK were subject to this six-month quarantine. During 2010, 82,512 dogs, 7,870 cats, and 64 ferrets entered the UK through PETS. In total, 752,945 animals, including those returning from trips abroad, have entered the UK under this scheme since 2000, and there have been no cases of rabies in any of these animals.

Comprehensive vaccination campaigns in foxes have helped to eliminate sylvatic rabies in many EU MSs; however, there is a constant threat of reintroduction through the importation of animals incubating the disease, especially from rabies endemic countries, considering the increasing trend in the noncommercial movement of animals around the world. Hence MSs need to maintain vigilance using appropriate control measures.[4] In 2004, the EU implemented a harmonized pet movement policy (referred to here as the EUPMP) under EU regulation 998/2003. The UK (and a number of other EU MSs) was granted derogation from this policy, initially due to expire in July 2008, but later extended until December 2011. Under the EUPMP, companion animals can move between EU MSs and into the EU from listed third countries providing they have been identified (either by tattoo or microchip), vaccinated against rabies, and have completed a 21-day waiting period before movement between countries ($EUPMP_{EU\&listed}$). Companion animals from unlisted third countries must be identified, vaccinated, serologically tested, and must complete a three-month waiting period in the country of origin after testing before entry into an EU MS ($EUPMP_{unlisted}$). A comparison of the various schemes is given in Table I.

If the UK's derogation from the EUPMP were to expire in December 2011, PETS and quarantine could be replaced by $EUPMP_{EU\&listed}$ and $EUPMP_{unlisted}$, respectively.[5] It was therefore considered prudent to assess the impact of this potential change in policy on the risk of rabies entering the UK due to the movement of companion animals so that an evidence base can be collected to help inform government policy decisions. To this effect, a quantitative risk assessment (QRA) model was developed to address the following risk questions: (i) How would the risk of rabies introduction to the UK via traveling companion animals change if the UK were to apply the current harmonized EU rules for the noncommercial movement of pets? (ii) How would the risk of rabies introduction from all countries change when rules are followed with 100% compliance or with varying degrees of less than 100% compliance? The resulting QRA developed was based on previous models constructed for companion animal entries from North America and Turkey;[6,7] however, the methodologies were substantially extended to consider entries from all countries. The outputs from the model are the annual probability of at least one companion animal that is incubating rabies virus entering the UK and the number of years between rabies introductions to the UK. Ferrets are not included in the model as (compared to dogs and cats) only a small

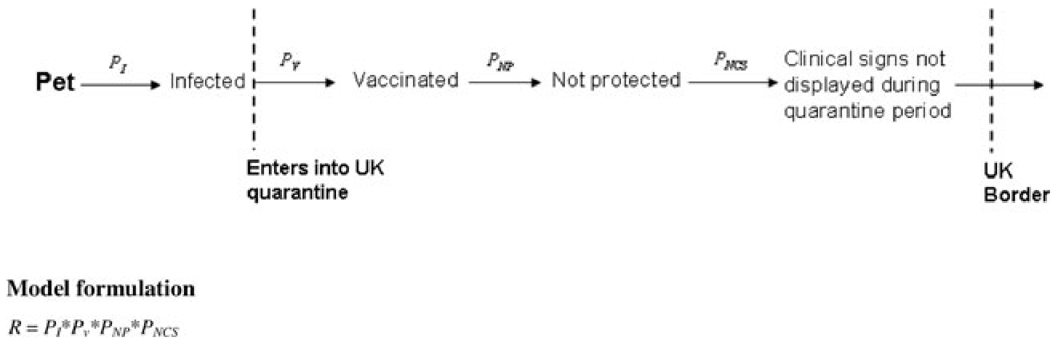


Fig. 1. The pathway used to model the risk of rabies introduction to the United Kingdom (UK) through six months in UK quarantine.

number enter the UK each year and there are very few data available relating specifically to rabies in ferrets.

2. MATERIALS AND METHODS

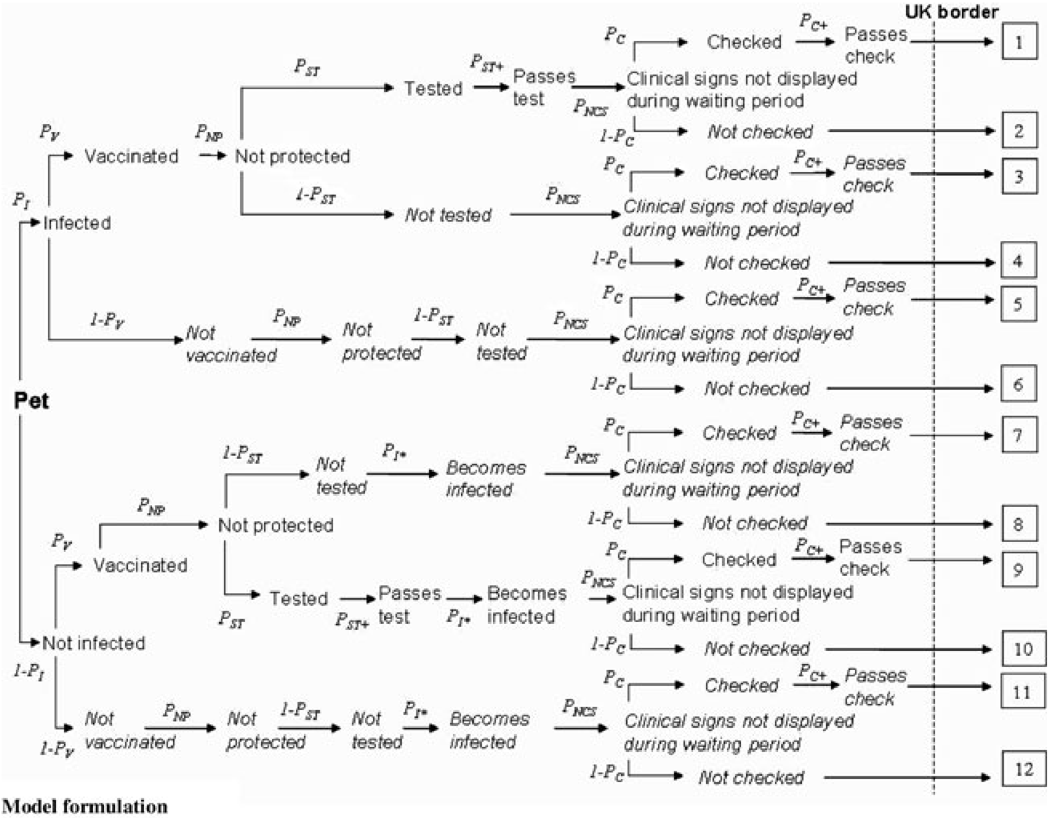
2.1. Risk Pathways

A risk pathway is required to identify the biological sequence of events that must take place in order for the hazard (i.e., rabies) being modeled to occur; in this case, the risk of at least one cat/dog incubating rabies virus entering the UK. The pathways for rabies importation to the UK used in this QRA, adopted from those in Ramnial *et al.*,[7] are given in Figs. 1–3. These pathways assume that animals that are infected with rabies virus, but yet to show clinical signs, are the only source of rabies introduction to the UK. Any animals displaying clinical signs of rabies before entry would be detected and removed from the scheme.

2.2. Country Groupings

The QRA is on a worldwide scale (i.e., not just restricted to a few countries/regions). Under PETS (and the EUPMP) all countries are assigned (according to EU regulation 998/2003) to one of three categories: EU MSs (and equivalents), listed third countries, and unlisted third countries. However, it is recognized that there is significant variability between countries within these categories in relation to the prevalence/incidence of rabies in their dog, cat, and wildlife populations. Therefore, countries were grouped within these three categories according to their annual number of reported rabies cases, thus overcoming the need to model each country individually. This also allowed for consideration of those countries for which these data on rabies cases and/or the animal population were either incomplete or absent. The concept of grouping countries has been used in many previous rabies risk assessments.[8,9]

To aid in grouping the countries, quantitative data on the number of reported rabies cases in dogs and cats in each country were assimilated from a number of sources.[10–12] Where possible, rabies cases in wild animals were kept separate from those in domestic dogs and cats to derive the most accurate number of rabies cases in animals that would be likely to travel internationally. Data were collected for the three-year period, 2007–2009, to collate the most recent data reporting rabies cases including the year-to-year variation. The individual countries within each of the three categories (EU MSs, listed third countries, and unlisted third countries) were collected into three groups, giving nine groups in total. The three within category risk groups were defined as follows: Group 1, no reported cases of rabies in cats, dogs, and wildlife during 2007–2009; Group 2, less than or equal to five total cases reported in cats and dogs during 2007–2009 and/or rabies present in wildlife; Group 3, greater than five cases reported in cats and dogs during 2007–2009. It was considered particularly important that countries with rabies in their wildlife population (not including lyssavirus species 2–11 in bats), but with no or very few cat/dog cases (from spill over events), be separated from those countries with no reports of rabies and those with a high number of rabies cases in domestic animals, hence the inclusion of Group 2. After collection of the incidence data and discussion with relevant experts, the threshold of five cases was selected as an appropriate value to use to differentiate between these two country groups. Countries for which quantitative data on rabies cases were incomplete or unavailable were assigned to



Model formulation

$R_1 = P_I*P_V*P_{NP}*P_{ST}*P_{ST+}*P_{NCS}*P_C*P_{C+}$
$R_2 = P_I*P_V*P_{NP}*P_{ST}*P_{ST+}*P_{NCS}*(1-P_C)$
$R_3 = P_I*P_V*P_{NP}*(1-P_{ST})*P_{NCS}*P_C*P_{C+}$
$R_4 = P_I*P_V*P_{NP}*(1-P_{ST})*P_{NCS}*(1-P_C)$
$R_5 = P_I*(1-P_V)*P_{NP}*(1-P_{ST})*P_{NCS}*P_C*P_{C+}$
$R_6 = P_I*(1-P_V)*P_{NP}*(1-P_{ST})*P_{NCS}*(1-P_C)$

$R_7 = (1-P_I)*P_V*P_{NP}*(1-P_{ST})*P_{I\bullet}*P_{NCS}*P_C*P_{C+}$
$R_8 = (1-P_I)*P_V*P_{NP}*(1-P_{ST})*P_{I\bullet}*P_{NCS}*(1-P_C)$
$R_9 = (1-P_I)*P_V*P_{NP}*P_{ST}*P_{ST+}*P_{I\bullet}*P_{NCS}*P_C*P_{C+}$
$R_{10} = (1-P_I)*P_V*P_{NP}*P_{ST}*P_{ST+}*P_{I\bullet}*P_{NCS}*(1-P_C)$
$R_{11} = (1-P_I)*(1-P_V)*P_{NP}*(1-P_{ST})*P_{I\bullet}*P_{NCS}*P_C*P_{C+}$
$R_{12} = (1-P_I)*(1-P_V)*P_{NP}*(1-P_{ST})*P_{I\bullet}*P_{NCS}*(1-P_C)$

$$R = \sum_{n=1}^{12} R_n \quad \text{where } n = \text{pathway index}$$

Fig. 2. The pathway used to model the risk of rabies introduction to the United Kingdom through the Pet Travel Scheme (PETS) and the European Union Pet Movement Policy for unlisted countries ($EUPMP_{unlisted}$). Illegal pathways are highlighted in italics.

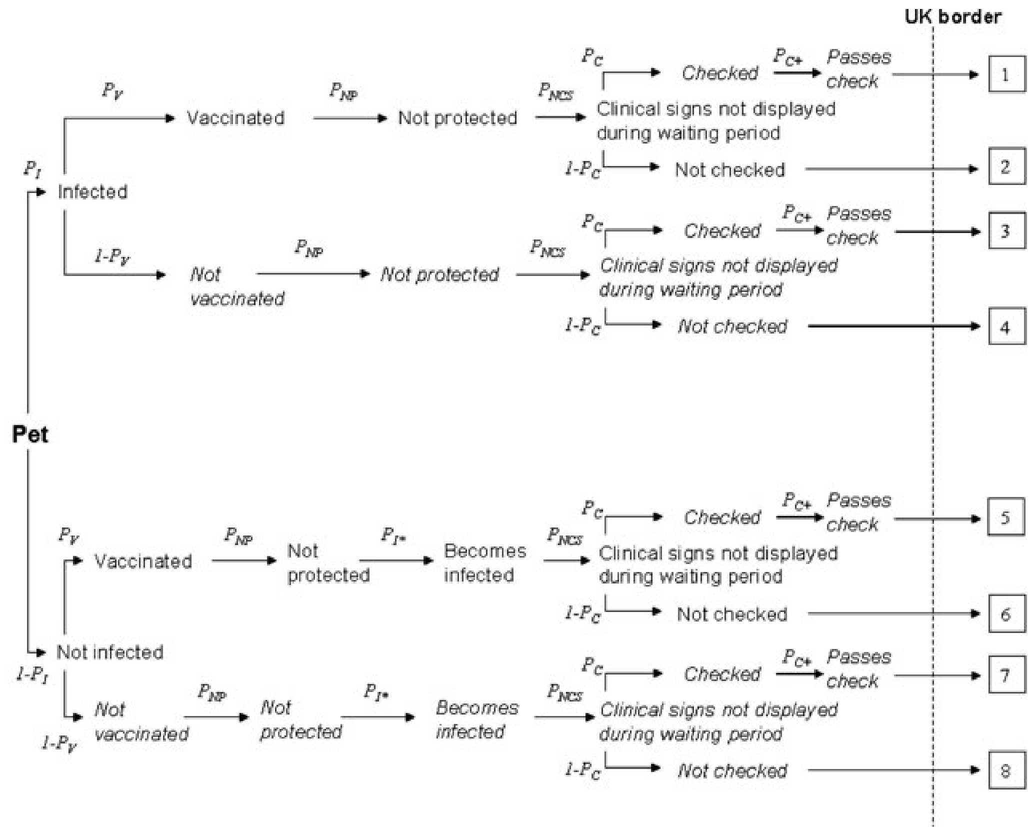
Groups 1–3 according to their classification of "No Risk," "Low Risk," or "High Risk" in a Health Protection Agency (HPA) assessment of the rabies risk to UK travelers,[13] which is based on rabies cases in all terrestrial animals. For countries where data are available, the HPA distinction between "Low Risk" and "High Risk" is broadly in agreement with our cut-off value of five cases between Group 2 and Group 3.

2.3. Parameter Estimation

The probabilities in Figs. 1–3 were estimated using data from published and unpublished research, government databases, and, where necessary, expert opinion. Many of the parameters in the pathways are specific to each country group. Where appropriate, the subscript j, $j = 1 \ldots 9$, was used to represent these groups: EU MSs (j = 1, 2, 3), listed countries (j = 4, 5, 6), and unlisted third countries (j = 7, 8, 9). The parameter values are presented with associated uncertainty; variability was not considered in the model.

2.3.1. Incubation Period of Rabies (IP)

The incubation period of rabies virus can be estimated from data on experimentally infected and/or naturally infected cases of rabies;[8,14–22] however, there is a large amount of uncertainty associated with both types of data (e.g., unknown date of infection in natural cases and potentially different incubation



Model formulation

$R_1 = P_I{*}P_V{*}P_{NP}{*}P_{NCS}{*}P_C{*}P_{C+}$ | $R_5 = (1\text{-}P_I){*}P_V{*}P_{NP}{*}P_{I*}{*}P_{NCS}{*}P_C{*}P_{C+}$

$R_2 = P_I{*}P_V{*}P_{NP}{*}P_{NCS}{*}(1\text{-}P_C)$ | $R_6 = (1\text{-}P_I){*}P_V{*}P_{NP}{*}P_{I*}{*}P_{NCS}{*}(1\text{-}P_C)$

$R_3 = P_I{*}(1\text{-}P_V){*}P_{NP}{*}P_{NCS}{*}P_C{*}P_{C+}$ | $R_7 = (1\text{-}P_I){*}(1\text{-}P_V){*}P_{NP}{*}P_{I*}{*}P_{NCS}{*}P_C{*}P_{C+}$

$R_4 = P_I{*}(1\text{-}P_V){*}P_{NP}{*}P_{NCS}{*}(1\text{-}P_C)$ | $R_8 = (1\text{-}P_I){*}(1\text{-}P_V){*}P_{NP}{*}P_{I*}{*}P_{NCS}{*}(1\text{-}P_C)$

$$R = \sum_{n=1}^{8} R_n \quad \text{where } n = \text{pathway index}$$

Fig. 3. The pathway used to model the risk of rabies introduction to the United Kingdom through the European Union Pet Movement Policy for EU and listed countries ($\text{EUPMP}_{\text{EU\&listed}}$). Illegal pathways are highlighted in italics.

periods in experimentally infected animals depending on the dose and route of infection). Therefore, similar to previous risk assessments[6,7] all available data sets were grouped and a lognormal distribution was fitted to the data; newly available data were incorporated to improve the estimate given in Jones *et al*.[6] This new lognormal distribution has a mean of 35 days and standard deviation of 36.8 days.

2.3.2. Probability Companion Animal from Country Group *j* is Infected ($P_{I,j}$)

For each country group j, $j = 1 \dots 9$, the probability of a companion animal being infected with rabies was estimated by considering the maximum number of rabies cases and the cat and dog population of countries for which both of these data were available. For each country within group $j, j = 1 \dots 9$, the maximum number of rabies cases over the period 2007–2009 was used to represent the current worse-case scenario, assuming no underreporting of rabies. These values were summed to give the maximum yearly number of rabies cases in each country group ($I_j, j = 1 \dots 9$; see Table II). The maximum number of unobserved rabies cases in a country group (α_j) was calculated as:[7]

$$\alpha_j = \frac{\overline{IP}}{365} \times I_j,$$

where $\overline{IP}$ is the mean incubation period (35 days). It was assumed that new cases of rabies in a country group j follow a Poisson process with rate λ_j.[6]

Table II. The Maximum Yearly Number of Rabies Cases in Each Country Grouping Used in the Risk Assessment (I_j);[10–12] Group 1, No Reported Cases of Rabies in Cats, Dogs, and Wildlife During 2007–2009; Group 2, Less than or Equal to Five Total Cases Reported in Cats and Dogs During 2007–2009 and/or Rabies Present in Wildlife; Group 3, Greater than Five Cases Reported in Cats and Dogs During 2007–2009

	European Union Member States (j = 1–3)	Listed Third Countries (j = 4–6)	Unlisted Third Countries (j = 7–9)
Group 1	0	0	0
Group 2	11	2	0[a]
Group 3	283	1,689	6,765

[a]Few data were available on rabies cases in unlisted third countries; however, a number of countries were placed in Group 2 due to their "Low Risk" classification in a Health Protection Agency risk assessment.

Using Bayesian inference, the uncertainty associated with λ_j was derived by assuming an uninformed "flat" prior[23] and a Poisson likelihood. The resulting posterior distribution for λ_j describes the uncertainty associated with the number of unobserved cases. This posterior distribution is given by:

$$\lambda_j \sim \text{Gamma}(\alpha_j + 1, 1).$$

The probability that a dog/cat from country group j is infected ($P_{I,j}$) was then estimated by dividing λ_j by the total cat and dog population of the countries in that group for which data on both the number of rabies cases and the dog and cat population (obtained from the World Society for the Protection of Animals (WSPA) and WAHID) were available. It was assumed that the estimate (and uncertainty distribution) for each grouping is representative of countries within the group for which data on the number of rabies cases and/or the companion animal population were unavailable.

2.3.3. *Probability that a Vaccinated Pet is not Protected (P_{NP})*

For this parameter the current OIE guidelines were used, which dictate that if an animal has a neutralizing antibody titer ≥0.5 international units (IU) per mL then it is considered to be protected, otherwise it is unprotected. Data were available on the efficacy of three rabies vaccines (Rabisin (Rb), Merial, France; Madivak (Md), Hoechst, Germany; Nobivak (Nb), Intervet, UK) from a number of experimental studies on the serological response of dogs and cats after vaccination,[24–27] see Table III. For each study and vaccine, the results were corrected to account for a serological test specificity of <100%, using a negative binomial distribution to estimate the number of false-positive animals,[28] thus giving the number of animals that were truly protected ($N_{V+,m}$) in each study (m):

$$N_{V+,m} = s_{V,m} - \text{NegBin}(s_{V,m} + 1, Sp_m),$$

where $s_{V,m}$ is the number of animals achieving the threshold titer and Sp_m is the specificity of the serological test used in study m. Data on the vaccine Rabisin were available from four studies; therefore, the probability of protection after vaccination with Rabisin (P_{Ra+}) was estimated by combining these data using Bayesian inference with an uninformed prior Beta(1,1) giving:

$$P_{Ra+} = \text{Beta}\left(\sum_{m=1}^{4} n_{Ra+,m} + 1, \sum_{m=1}^{4} N_{Ra,m} - \sum_{m=1}^{4} n_{Ra+,m} + 1\right),$$

where $N_{Ra,m}$ is the number of animals vaccinated with Rabisin in study m and $n_{Ra+,m}$ is the number of animals that are truly protected after vaccination with Rabisin in study m. Only one data set was available for both Madivak and Nobivak; therefore, the

Table III. Data used to Estimate the Probability of an Animal Not Being Protected from Rabies Infection After Being Administered a Rabies Vaccine (P_{NP})

Study Number (m)	Reference	Vaccine Used (V)	Days Between Vaccination and Testing	Number of Animals Tested ($N_{V,m}$)	Serological Test Used	Number Achieving Threshold Titer of >0.5 IU/mL ($s_{V,m}$)
1	Sihvonen *et al.* (1995)	Rabisin	30–40	83	RFFIT	80
		Madivak		47		46
2	Kallel *et al.* (2006)	Rabisin	30	5	RFFIT	4
3	Bahloul *et al.* (2006)	Rabisin	35	4	RFFIT	4
4	Minke *et al.* (2009)	Rabisin	28	15	FAVN	14
		Nobivak		15		10

probability of protection after vaccination with these vaccines was estimated by:

$$P_{V+} = \text{Beta}(n_{V+} + 1, N_V - n_{V+} + 1),$$

where V = Md, Nb. Limited information is available on the frequency of use of each vaccine, especially in countries outside the UK; therefore, assuming each vaccine is used with the same frequency, the probability of a cat/dog not being protected (P_{NP}) after vaccination was estimated from the available data on all three vaccines, giving an average probability that a rabies vaccine will not induce protection:

$$P_{NP} = 1 - \frac{P_{Rb+} + P_{Md+} + P_{Nb+}}{3}.$$

The mean value for this parameter was 0.186; however, this value only applies to animals not incubating rabies. For animals that are incubating rabies virus or have not been vaccinated, P_{NP} is assumed to equal 1.

2.3.4. *Probability that an Unprotected Animal Passes the Serological Test (P_{ST+})*

Companion animals intending to enter the UK via PETS or $\text{EUPMP}_{\text{unlisted}}$ should only be allowed to proceed through the scheme if they are protected from rabies infection (i.e., have an antibody titer ≥0.5 IU/mL). Unprotected animals should not pass this test. However, it is unlikely that any test will be 100% specific; therefore, a small proportion of unprotected animals may pass the test and be allowed to proceed through the scheme. The average specificity of the serological tests for rabies antibodies was estimated from published data comparing the Fluorescent Antibody Virus Neutralization (FAVN) test and the Rapid Fluorescent Focus Inhibition Test (RFFIT).[29] A Bayesian model[30] was fitted to the FAVN data using WinBUGS 1.4 software, assuming that the antibody prevalence in vaccinated dogs would be high, and low in unvaccinated dogs. Uninformative Beta(1,1) priors were used for the FAVN specificity and sensitivity. A similar model was fitted to the RFFIT data; however, for the sensitivity and specificity of the FAVN test and the antibody prevalences, the prior Beta distributions were based on the parameter estimates from the FAVN model. The results from these models were used to define Beta distributions for the FAVN (Sp_{FAVN}) and RFFIT (Sp_{RFFIT}) specificities. Given the limited information on the frequency of use of each test these values were equally weighted to produce an average specificity of the serological tests for rabies antibodies (Sp), a mean value of 0.968 in the model. The probability of an unprotected animal passing the serological test (P_{ST+}) is thus:

$$P_{ST+} = 1 - Sp.$$

The serological test results were not corrected for a sensitivity of <100%; protected animals that test negative for rabies-virus-specific antibodies will either be revaccinated and retested or removed from the scheme; therefore, these animals do not influence the risk of rabies introduction to the UK.

2.3.5. *Probability that an Unprotected Animal Becomes Infected During Waiting Period ($P_{I*,j}$)*

Companion animals that are not protected after vaccination, or those that have not been vaccinated, may become infected during the waiting period. This probability was estimated as:

$$P_{I^*,j} = 1 - (1 - P_{I',j})^T,$$

where $P_{I',j}$ is the daily probability of a companion animal in group j becoming infected and T is the total waiting period for each scheme (212 days for PETS, 121 days for $\text{EUPMP}_{\text{unlisted}}$, and 21 days for $\text{EUPMP}_{\text{EU\&listed}}$; a one-month wait is assumed between vaccination and testing in PETS and $\text{EUPMP}_{\text{unlisted}}$). The probability of an animal becoming infected while in UK quarantine was not considered.

The estimate of $P_{I',j}$ was based on the maximum annual number of rabies cases in companion animals between 2007 and 2009 (I_j). Firstly, as for λ_j, the uncertainty associated with this number of cases (θ_j) was estimated as:

$$\theta_j \sim \text{Gamma}(I_j + 1, 1).$$

$P_{I',j}$ was then estimated as:

$$P_{I',j} = \frac{\theta_j}{N_j^* 365},$$

where N_j is the combined cat/dog population of group j. Noncompliant animals are assumed to be moved into the UK with false documentation after one day; therefore, in these situations $P_{I^*,j} = P_{I',j}$.

2.3.6. *Probability that an Infected Animal is Asymptomatic During the Waiting Period (P_{NCS})*

It was assumed that companion animals displaying clinical signs of rabies would not be allowed to enter the UK. However, animals that are incubating the disease and do not show clinical signs during the waiting period may enter the country. This probability is dependent on the time between infection and entry (t) and the incubation period (IP). For animals infected before vaccination, the time between infection and entry is dependent on the waiting period (T) of the entry scheme, assuming that the animal was infected immediately before vaccination and enters the country immediately after the waiting period. The probability of the incubation period being greater than the waiting period in a particular entry scheme (P_{NCS}) was calculated from the cumulative density function of the lognormal distribution describing the incubation period:

$$P_{NCS} = P(IP > T),$$

where T is the total waiting period as described previously.

For unprotected animals that become infected during the waiting period, infection could occur on any day between the day of vaccination ($t = 1$) and the day of entry ($t = T$). The probability of an animal that becomes infected during the waiting period not displaying clinical signs during the waiting period was calculated by averaging the associated probabilities for each possible day of infection, that is,

$$P_{NCS} = \frac{\sum_{t=1}^{T} P(IP > t)}{T}.$$

2.3.7. *Probability an Animal Passes Import Checks from a Country Group j ($P_{C+,j}$)*

Upon arrival at a UK border, a companion animal may be denied entry if the accompanying paperwork is unsatisfactory. Data on the number of companion animals presented for entry to the UK ($N_{C,j}$) and the number that were subsequently allowed to enter ($n_{C+,j}$) were collated from pet travel records in the UK; see Table IV. For each country group ($j = 1, \ldots, 6$) entering via PETS, the probability of an animal from that group passing documentation checks upon entry to the UK was therefore estimated as:

$$P_{C+,j} = \text{Beta}(n_{C+,j} + 1, N_{C,j} - n_{C+,j} + 1).$$

Table IV. The Number of Companion Animals Passing Entry Checks into the United Kingdom Between 2005 and 2009[33]

Country Classification	Country Group	Number Presented ($N_{C,j}$)	Number Passing Checks ($N_{C+,j}$)
EU Member States and equivalents	Group 1	63,863	59,877
	Group 2	91,056	85,662
	Group 3	7,652	6,157
Listed third countries	Group 1	7,280	7,184
	Group 2	2,206	2,150
	Group 3	19,442	17,631

Data are not available for the number of entries from unlisted third countries failing UK entry checks, as these entries currently go through six-month quarantine. Therefore, for these countries under the EUPMP, the probability of passing import checks was estimated using a Beta distribution incorporating all the data on animals passing and failing checks upon entry into the UK.

2.3.8. *Compliance Parameters*

Noncompliance with the regulations was modeled at the vaccination, testing, and checking stages of the pathways (see Figs. 2 and 3) by altering the probabilities of an animal being vaccinated, serologically tested, and checked, parameters P_V, P_{ST}, and P_C, respectively. In the baseline model, 100% compliance was assumed; therefore, $P_V = 1$ and $P_{ST} = 1$. In PETS, all companion animal entries must be checked; therefore, in this case $P_C = 1$. Under the EUPMP, entries into the EU must be checked; therefore, $P_C = 1$ for entries from unlisted third countries in $\text{EUPMP}_{\text{unlisted}}$ and entries from listed third countries in $\text{EUPMP}_{\text{EU\&listed}}$. There is not any requirement for checking the movements of companion animal movements between EU MSs in the EUPMP; therefore, in these cases $P_C = 0$.

The effect of noncompliance with the regulations on the risk of rabies introduction to the UK was tested in a scenario analysis where the compliance parameters were reduced, in a stepwise manner, to 0.9 (90% compliance) and then to 0.8 (80% compliance). This reduction in compliance did not affect the parameter P_V in UK quarantine, where it was assumed that all regulations were complied with, or P_C in movements between MSs in the EUPMP, which remains at 0 in the compliance analysis. For animals that were either not vaccinated or not tested, it was

Table V. The Maximum Annual Number of Companion Animal Entries to the United Kingdom via the Pet Travel Scheme (PETS) and Quarantine ($N_{I,j}$) Between 2005 and 2009[33]

	European Union Member States		Listed Third		Unlisted Third
Country Group	PETS (%)	Quarantine (%)	PETS (%)	Quarantine (%)	Quarantine (%)
Group 1	13, 434(97%)	423(3%)	2, 657(92%)	217(8%)	22(100%)
Group 2	19, 830(98%)	403(2%)	859(88%)	121(12%)	51(100%)
Group 3	1, 740(97%)	52(3%)	5, 091(86%)	819(14%)	1, 222(100%)

assumed that they will attempt to enter the UK immediately with false documentation ($T = 1$ for these entries). In addition, it was assumed that those animals that had not been vaccinated and will not be tested for rabies antibodies; therefore, $P_{\mathrm{ST}} = 0$ in these scenarios.

2.3.9. *Companion Animal Entries to the UK*

The annual number of companion animal entries to the UK from each of the nine country groups was obtained from pet travel records (Table V). The maximum number of entries over the last five years was selected to model a worse-case scenario for companion animal entries, and therefore rabies introduction. It was noted that during this time frame a substantial number of animals entered the UK from PETS qualifying countries via quarantine. It is speculated that these may be cats/dogs whose owners have, for whatever reason, decided to forgo PETS (likely to be those not wishing to wait for six months before entering the UK) or cats/dogs that have been placed in quarantine because they have failed the requirements for PETS. When modeling the current UK scheme, these animals were assumed to enter through a full six-month quarantine period; early release cases were not included in the model. For the EUPMP, entries through quarantine from qualifying countries (EU and listed) were grouped with the number of entries through PETS to give an overall annual number of entries; all of these were assumed to enter through $\mathrm{EUPMP}_{\mathrm{EU\&listed}}$. This assumption was made because under the EUPMP there is likely to be no option for quarantine, and it was considered more likely that owners will be willing to wait 21 days before entry. For both schemes, it is assumed that all animals are entering the UK for the first time and all animals have fulfilled the requirements and completed the full waiting period immediately before entry.

In this QRA, the risk of rabies introduction from UK animals returning from abroad was not considered due to the lack of central recording of these specific movements. However, it is considered that the risk posed to the UK from domestic UK animals becoming infected while abroad would be very low compared to the risk from animals entering the UK from abroad. This is because the majority of trips are likely to be relatively short in duration and most traveling animals would be expected to have only minimal contact with the local cat and dog population. Furthermore, if the animals are fully compliant with the vaccination requirements, there is a high probability the animal is protected from clinical infection even given exposure to the virus.

2.4. Estimation of Risk

For each pet movement policy (quarantine, PETS, $\mathrm{EUPMP}_{\mathrm{unlisted}}$, and $\mathrm{EUPMP}_{\mathrm{EU\&listed}}$) and country grouping, the probability of a single pet being infected and imported (R), which is scenario specific, was estimated by summing the probabilities associated with each pathway in the relevant risk pathway diagram (Figs. 1–3). Consequently, the annual probability of importing at least one infected cat/dog ($P_{\mathrm{R},j}$) via a particular scheme for country group j was estimated by:

$$P_{\mathrm{R},j} = 1 - (1 - R)^{N_{I,j}},$$

where $N_{I,j}$ is the number of pets imported via the particular scheme for country group j; see Table V. Therefore, the number of years between rabies introductions from a particular group ($Y_{\mathrm{R},j}$) was estimated as:

$$Y_{\mathrm{R},j} = \frac{1}{P_{\mathrm{R},j}}.$$

The probabilities of at least one infected animal entering the UK via a particular scheme from either an EU MS, listed third country, or an unlisted third

Table VI. Results: Annual Probability of Rabies Introduction to the United Kingdom (P_R) via the Pet Travel Scheme (PETS) and the European Union Pet Movement Policy (EUPMP)

Country Category	Scenario	Compliance Level	5th Percentile	Mean	95th Percentile
EU MSs	PETS/Quarantine	100%	3.43×10^{-6}	8.34×10^{-6}	1.60×10^{-5}
	$\text{EUPMP}_{\text{EU\&listed}}$	100%	1.41×10^{-3}	2.02×10^{-3}	2.79×10^{-3}
Listed third countries	PETS/Quarantine	100%	1.32×10^{-5}	2.64×10^{-5}	4.69×10^{-5}
	$\text{EUPMP}_{\text{EU\&listed}}$	100%	2.39×10^{-3}	2.75×10^{-3}	3.15×10^{-3}
Unlisted third countries	Quarantine	100%	3.91×10^{-5}	4.31×10^{-5}	4.82×10^{-5}
	$\text{EUPMP}_{\text{unlisted}}$	100%	9.47×10^{-6}	2.58×10^{-5}	5.05×10^{-5}
Overall	PETS/Quarantine	100%	5.90×10^{-5}	7.79×10^{-5}	1.06×10^{-4}
	PETS/Quarantine	90%	1.12×10^{-3}	1.33×10^{-3}	1.58×10^{-3}
	PETS/Quarantine	80%	2.08×10^{-3}	2.48×10^{-3}	2.97×10^{-3}
	EUPMP	100%	4.05×10^{-3}	4.79×10^{-3}	5.65×10^{-3}
	EUPMP	90%	5.13×10^{-3}	5.92×10^{-3}	6.85×10^{-3}
	EUPMP	80%	6.13×10^{-3}	6.99×10^{-3}	7.99×10^{-3}

country were given by:

$$P_{\text{R,EU}} = 1 - (1 - P_{\text{R},1})(1 - P_{\text{R},2})(1 - P_{\text{R},3}),$$

$$P_{\text{R,listed}} = 1 - (1 - P_{\text{R},4})(1 - P_{\text{R},5})(1 - P_{\text{R},6}),$$

$$P_{\text{R,unlisted}} = 1 - (1 - P_{\text{R},7})(1 - P_{\text{R},8})(1 - P_{\text{R},9}).$$

The number of years between introductions from each country classification is calculated by dividing 1 by these probabilities, that is, $1/P_{\text{R,EU}}$, $1/P_{\text{R,listed}}$, and $1/P_{\text{R,unlisted}}$. Therefore, the overall annual probability of at least one infected dog/cat entering the UK is:

$$P_{\text{R}} = 1 - (1 - P_{\text{R,EU}})(1 - P_{\text{R,listed}})(1 - P_{\text{R,unlisted}}),$$

where the overall number of years between rabies introductions is $1/P_{\text{R}}$.

2.5. Model Implementation

The model was developed in the software package @Risk Version 4.5 (©Palisade), an add-on package within Microsoft Excel 2003 (©Microsoft 1985–2003). Each simulation was run for 50,000 iterations, which was sufficient to allow convergence of the annual risk of rabies introduction (P_{R}). The results presented follow the standard form of the arithmetic mean and the 5th and 95th percentile values.

2.6. Sensitivity and Scenario Analysis

A sensitivity analysis was conducted using the software in @Risk. The analysis identifies, from those represented by a distribution, the model parameters the results are most sensitive to, that is, which inputs contribute most to the output uncertainty. In addition to this analysis, some alternative scenarios are tested to assess how the risk associated with PETS scheme is affected by the individual requirements of the policy. First the consequence of removing the serological test requirement from PETS is assessed by changing the probability of passing the test ($P_{\text{ST+}}$) to 1. Second, the effect of a reduced waiting period in PETS is assessed by reducing T in monthly intervals, from 212 days in the baseline model to 1 day, which is effectively immediate entry (i.e., $T = 212, 180, 150 \ldots 1$).

3. RESULTS

The annual probability of rabies introduction to the UK through PETS /quarantine and EUPMP is shown in Table VI. Under the current companion animal movement policy of PETS and quarantine, the annual probability of rabies introduction is 7.79×10^{-5} (5.90×10^{-5}, 1.04×10^{-4}), with introduction from unlisted third countries through quarantine contributing the highest risk of 4.31×10^{-5} (3.91×10^{-5}, 4.82×10^{-5}). This is because the extra elements of the PETS scheme (on top of the six-month wait) result in PETS being a "safer" scheme than quarantine alone. Under the EUPMP, the annual probability of rabies introduction is predicted to be higher at 4.79×10^{-3} (4.05×10^{-3}, 5.65×10^{-3}). Interestingly, the results indicate that companion animal entries from EU MSs and listed third countries contribute the most risk under the EUPMP, whereas the risk of rabies introduction from unlisted third countries is predicted to decrease compared to PETS/quarantine. These conclusions are taken from the mean values. However, when uncertainty is taken into

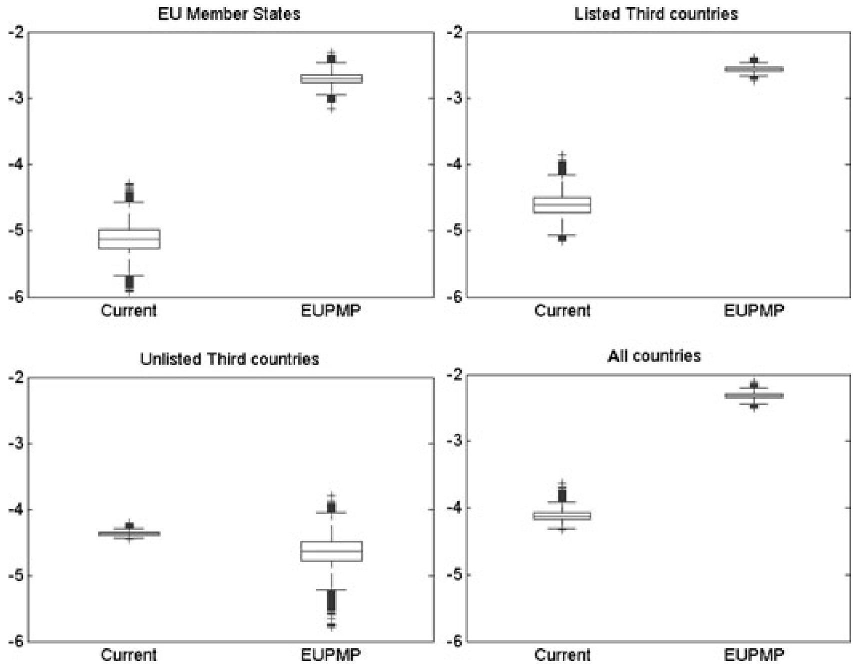


Fig. 4. Box plots comparing the annual risk of rabies introduction to the United Kingdom (UK) under the current Pet Travel Scheme (PETS) to the risk of introduction through the European Union Pet Movement Policy (EUPMP) for EU member states ($P_{R,EU}$), listed third countries ($P_{R,listed}$), unlisted third countries ($P_{R,unlisted}$), and all regions combined (P_R). Note: All *y*-axes are the log10 of the annual probability of rabies introduction to the UK.

consideration (Fig. 4) there is a much higher amount of uncertainty associated with the $EUPMP_{unlisted}$ scheme, with the percentiles fully encompassing the distribution of results in the quarantine scenarios. With respect to the number of years between rabies introductions, it is predicted that after a change in policy to the EUPMP, the overall number of years between rabies introductions would decrease from 13,272 (9,408, 16,940) to 211 (177, 247) years (Table VII).

As expected, when noncompliance is introduced to the model the risk of rabies introduction to the UK increases. The effect of this is most notable for the current scheme of PETS and quarantine, with a 20% reduction in compliance reducing the number of years between rabies introductions to 408 (337, 482) years. The effect of noncompliance is less under the EUPMP, with a decrease in the number of years between rabies introductions to 144 (125, 163) years if compliance is reduced by 20%.

A sensitivity analysis indicated that for PETS the risk of rabies entry is most sensitive to changes in the sensitivity and the serological test, the efficacy of the rabies vaccine, and the number of unobserved

Table VII. Results: Expected Number of Years Between Rabies Introduction to the United Kingdom (Y_R) via Either the Pet Travel Scheme (PETS) or the European Union Pet Movement Policy (EUPMP)

Country Category	Scenario	Compliance Level	5th Percentile	Mean	95th Percentile
EU MSs	PETS/Quarantine	100%	62,683	1,49,129	2,91,248
	$EUPMP_{EU\&listed}$	100%	359	517	708
Listed third countries	PETS/Quarantine	100%	21,299	43,942	75,973
	$EUPMP_{EU\&listed}$	100%	317	366	419
Unlisted third countries	Quarantine	100%	20,738	23,302	25,557
	$EUPMP_{unlisted}$	100%	19,792	50,440	1,05,590
Overall	PETS/Quarantine	100%	9,408	13,272	16,940
	PETS/Quarantine	90%	632	761	894
	PETS/Quarantine	80%	337	408	482
	EUPMP	100%	177	211	247
	EUPMP	90%	146	170	195
	EUPMP	80%	125	144	163

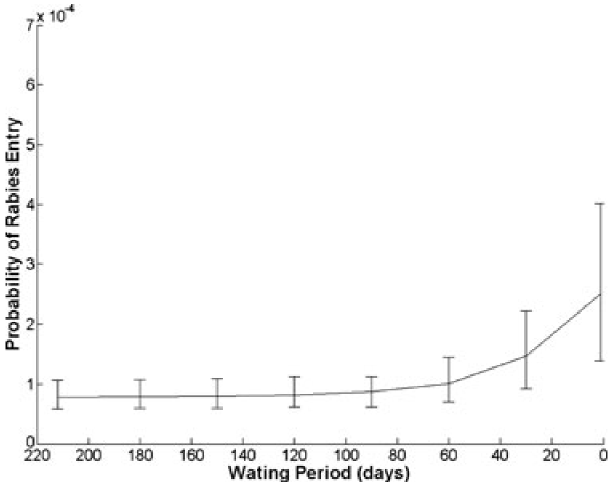


Fig. 5. The change in the probability of rabies introduction to the United Kingdom (P_R) through the Pet Travel Scheme as the total waiting period is reduced in monthly intervals from 212 days in the baseline model to a waiting period of 1 day, which is, in effect, immediate movement of all animals.

infected animals in unlisted countries (λ_j, j = 7–9). This result is likely to be because the majority of the risk associated with this scheme is through undetected infected animals entering the UK through quarantine. Similarly, for EUPMP the vaccine efficacy and the number of unobserved infected animals from EU MSs and listed third countries (λ_j, j = 1–6) contribute the most uncertainty to the overall risk, again because the majority of the risk associated with this scheme comes from these country groups.

In a scenario analysis, removing the serological test requirement from PETS increases the annual mean risk of rabies introduction approximately 10-fold to 9.17×10^{-4} (5.94×10^{-4}, 1.28×10^{-3}), and reduces the number of years between rabies introductions to 1,152 (780, 1682) years. A number of scenarios were considered where the waiting period for PETS was reduced in monthly intervals; these analyses showed that reducing the waiting period increased the risk of rabies introduction, particularly when the waiting period is less than three months (Fig. 5).

4. DISCUSSION

The UK has maintained its rabies-free status since 1922, initially by a six-month quarantine and since 2000 a combination of PETS and quarantine. The UK's derogation from harmonized EU laws relating to companion animal travel will expire in December 2011. The QRA presented here was designed to quantify any potential change in risk after harmonization with EU laws. Assuming that the annual number of companion animal entries is consistent at an average of 46,491, the model results indicate that under the current scheme of PETS and quarantine there would be, on average, one rabies introduction every 13,272 years, or one introduction every 617,028,552 animal entries. Therefore, it can be concluded that assuming 100% compliance with the regulations, the risk of rabies introduction to the UK under the current scheme is very low or negligible; this is consistent with the fact that the UK has remained rabies-free in the 10 years since the introduction of PETS. After adoption of the EUPMP, the mean risk of rabies introduction to the UK is predicted to increase by approximately 60-fold. It is predicted that, on average, there will be one rabies introduction every 211 years under the EUPMP, this is one introduction every 9,806,601 companion animal entries. Consequently, while an increase in the mean risk of rabies introduction is predicted after a policy change to the EUPMP, the absolute risk associated with both schemes is very low. This risk assessment differs from previous rabies risk assessments in that it considers entries to the UK from all countries in the world, as opposed to entries from only a single country or region. However, the conclusions from this risk assessment are consistent with previous assessments that have suggested that the EUPMP would pose a higher risk of rabies introduction compared to the current policy of PETS and quarantine[(7)] and that the removal of the serological test requirement from an entry scheme would increase the likelihood of rabies introduction,[(9)] particularly when the waiting period is also reduced.[(31)]

When the UK adopts the EUPMP it is predicted that companion animal entries from listed third countries would present the highest mean risk of rabies introduction to the UK, whereas the mean risk of rabies introduction from unlisted third countries would decrease. These results are supported by the conclusions made in a qualitative risk assessment undertaken by Defra,[(32)] which concluded that, under the EUPMP, there would not be any change to the current negligible risk of rabies introduction to the UK from unlisted third countries, but an increase to a very low risk of rabies introduction from listed third countries. The qualitative risk assessment also concluded that there would be no change to the risk of rabies introduction to the UK from EU MSs under the EUPMP; however, we predict an increase to one rabies-infected entry every 517 years (or one entry every 240,35,847 animals). Although this is almost a 300-fold increase in mean risk, the absolute level of risk could be considered negligible. When interpreting the results of this risk assessment, uncertainty must also be taken into consideration. A large amount of uncertainty is associated with the predicted risk of rabies introduction from unlisted third countries under the EUPMP (Fig. 4), the confidence intervals for this result completely encompass the equivalent results through quarantine. Therefore, although the mean results suggest a decrease in risk under the EUPMP, this conclusion is weakened by the extra uncertainty associated with the EUPMP results.

One of the main differences between PETS and the EUPMP is the length of the waiting period. A scenario analysis showed that reducing the waiting period of PETS to 90 days did not greatly increase the mean risk of rabies introduction. However, waiting periods shorter than 90 days resulted in a substantial increase in risk (Fig. 5). This is an important result as it suggests that the waiting period change between the PETS and $\text{EUPMP}_{\text{unlisted}}$ policies (from six to three months) would not substantially affect the mean risk of rabies introduction, but reducing the waiting period to 21 days (as in $\text{EUPMP}_{\text{listed}}$) would result in a large increase in risk.

The baseline model for this QRA assumes 100% compliance, that is, all animals had the correct vaccination and serological test. This approach was taken as the best available data for compliance indicated that the current level of compliance with the vaccination and serological test requirements is nearing 100% (only 796 of 191,499 animals (approximately 0.4%) failed to meet the entry requirements for these reasons between 2005 and 2009).[33] However, the effect of noncompliance on the risk of rabies introduction to the UK due to companion animal movements has been analyzed by reducing the level of compliance with the vaccination, serological testing, and border checking requirements of the schemes. Previous risk assessments have included noncompliance using uncertainty distributions;[6–8,34] however, these distributions were not used as they were published in 1998 before PETS was introduced, and were therefore deemed to not accurately represent the current level of compliance with PETS. Despite this change in methodology, the results of this QRA are in agreement with previous studies, indicating that the risk of rabies introduction to the UK, particularly via PETS, is highly sensitive to noncompliance with the regulations.[6,7] It is likely that the introduction of noncompliance to the model has a large effect due to the assumption of immediate movement into the UK of animals that were either not vaccinated against rabies or serologically tested for rabies antibodies.

During the development of this risk assessment, a number of assumptions had to be made either due to the lack of available data or the uncertainty associated with the available data. To model the overall risk of rabies introduction to the UK in a timely and efficient manner, the countries of the world were combined into groups based on their reported number of rabies cases between 2007 and 2009. The maximum number of annual rabies cases in each group over this period was used in subsequent calculations to account, to some degree, for underreporting. Following the definition of the groups, where both sets of quantitative data were available, the data on rabies cases were combined with the companion animal population for each country. In effect, each group was treated as one very large country, assuming that the average rabies prevalence would be representative of the overall rabies situation in all the countries in the group and that rabies-infected animals are homogenously distributed across the countries. Spatial heterogeneity of rabies cases, the quality of each country's veterinary surveillance system, and other factors that could affect the risk of rabies introduction to the UK could not be considered due to a lack of specific data in these areas.

The countries of the world were separated into three groups based on their number of reported rabies cases; where incidence data were not available a previous HPA rabies risk assessment was used to assist in categorization.[13] Due to a lack of data on the pet/wildlife population for each country, and the likely difference in the owner–animal ratio between countries, it was not possible to define the country groupings according to prevalence and incidence was used as a proxy. After discussion with rabies experts, a threshold of five cases was selected to differentiate between Group 2 and 3 countries. As a result of this some countries with relatively few rabies cases (6–10 between 2007 and 2009) will have been included in Group 3 along with countries with far greater number of rabies cases. A full breakdown of results for the individual country groups (not shown) indicates that the majority of risk comes from the Group 3 countries. Adjusting the Group 2–Group 3 threshold within a range of reasonable values (5–10 cases) would be unlikely to significantly affect the results and, if anything, the cautionary threshold used in the model leads to a worse-case scenario.

The proportion of uninfected pets that are protected from rabies after vaccination was based on data on the seroconversion of companion animals above a threshold antibody titer of 0.5 IU/mL, informed by the current EU, WHO, and OIE guidelines.[35] However, this is an arbitrary threshold that is not in accordance with criteria for licensing of vaccines for veterinary use, and it has been shown in some studies that the lack of neutralizing antibodies in vaccinated animals before challenge with rabies virus does not indicate that the animal is unprotected from rabies challenge,[36,37] thus meaning the value used in the risk assessment may be an underestimate, which may lead to an overestimate in the risk of rabies introduction. A scenario analysis (not shown) showed that an increase in the probability of a companion animals being protected after vaccination would decrease the risk of rabies introduction to the UK (an increase in vaccine efficacy to 0.9 reduced the risk associated with PETS/quarantine to 6.52×10^{-5}, or one rabies introduction every 15,496 years). However, the effect of this change in the parameter estimate would not affect the overall conclusions of this QRA or any subsequent policy decisions.

The estimate of the incubation period of rabies virus used in this QRA was based on data on both experimentally and naturally infected cases of rabies. The data were combined due to the high level of uncertainty associated with both data sets, due to high infectious doses in experimental cases and uncertainty about the true incubation period in naturally infected cases, because there was no knowledge of the true date of infection and the potential for secondary cases in data on rabies in UK quarantine. The true incubation period of rabies virus in dogs and cats, particularly naturally infected cases, is one of the key data gaps identified by this QRA. Data that would allow improved estimation of this parameter would be advantageous for an improvement to the estimation of risk in future rabies risk assessments, particularly as one of the important distinctions between the various entry policies is the length of the waiting period that must be completed before entry.

There has been a large increase in the number of companion animals entering the UK in the years since the introduction of PETS; in 1996, 7,267 cats and dogs were quarantined in the UK,[8] by 2009 this had increased to 30,268 entries via PETS with a further 1,099 entries through quarantine (these figures do not include UK animals returning from trips abroad). It was assumed that under the EUPMP there would be no further increase in the number of companion animal entries to the UK. However, it is possible that entry numbers would increase after a change to the EUPMP due to the simplification of the entry requirements, in which case the risk of rabies introduction to the UK would increase further. This may be particularly true for entries from unlisted countries, which would no longer be subject to the six-month quarantine system.

Finally, it should be noted that this risk assessment only considers the risk of rabies introduction to the UK via the movement of companion animals. No consideration was given to other imported diseases/infections that may be associated with dog/cat travel, in particular leishmaniois and *Echinococcus multilocularis*, which have been considered in other studies.[38,39] On June 30, 2011, the UK government announced that the UK pet importation policy would be harmonized with the EU and the EUPMP would be effective from January 1, 2012;[40] the results of this risk assessment formed part of the scientific evidence base in this policy decision.

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