EFSA Scientific Opinion on canine leishmaniosis

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European Food Safety Authority

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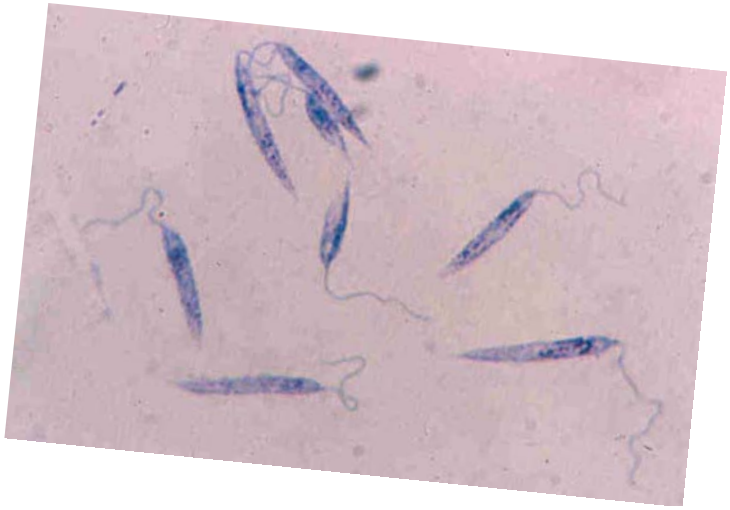
PRESENTATION OUTLINE

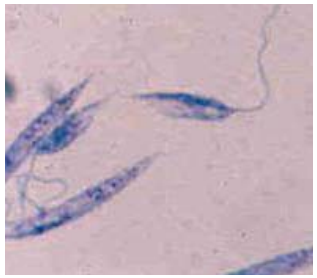
Outline



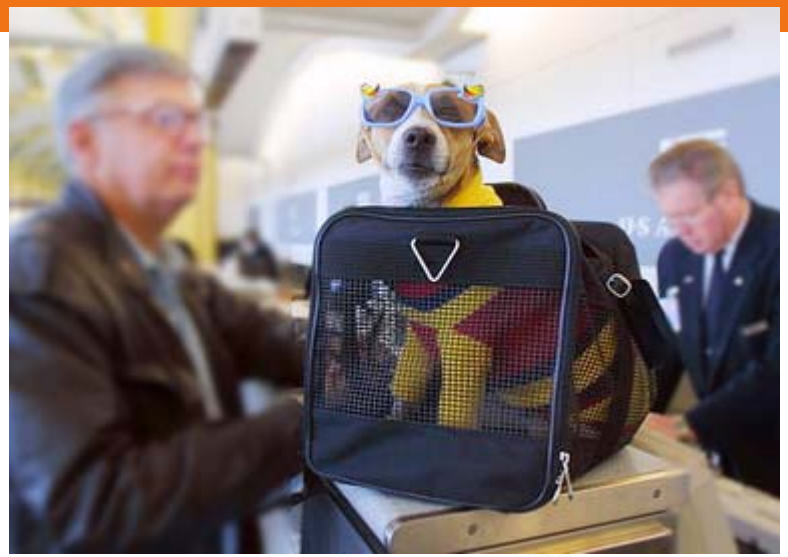
- Background
- ToR
- Approach
- Data and Methodologies
- Assessment
- Conclusions & Recommendations

BACKGROUND

- **Leishmaniosis**
  - parasitic disease of humans and animals
  - non-notifiable in animals
  - cutaneous and visceral form
  - protozoa of the genus *Leishmania*
  - *Leishmania infantum* in Mediterranean area
  - transmitted by sandflies (*Phlebotomus*)
  - domestic dogs principal reservoir hosts
    - efficiently replicate the protozoan parasite
    - preferred hosts for vector phlebotomine sandflies



BACKGROUND: TRAVELLING WITH DOGS



Published in European Urban and Regional Studies 1997 v 4(2) 115-134

A PLACE IN THE SUN: INTERNATIONAL RETIREMENT MIGRATION FROM NORTHERN TO SOUTHERN EUROPE

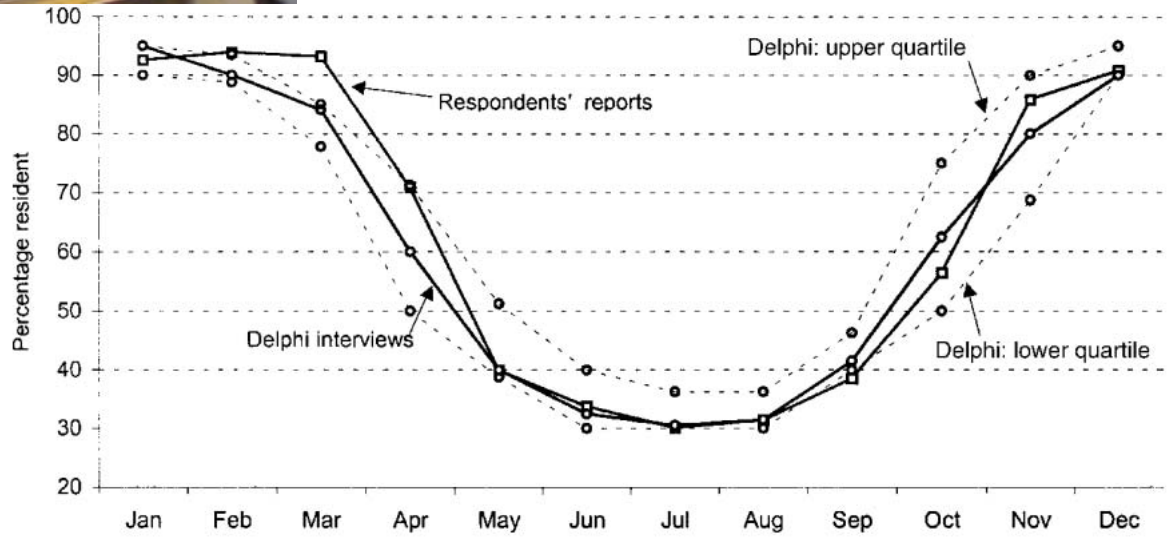


Figure 2. Seasonal pattern of residence of German retired people in the Canary Islands.

Source: http://dx.doi.org/10.1017/S0144686X04001898

TERMS OF REFERENCE

- **Characterise canine leishmaniosis in Europe and in particular:**
  - **epidemiology of the disease, i.e. affected species, life cycle, modes of transmission and potential persistence of the parasite, distribution of the disease (free and endemic areas);**
  - **impact of *Leishmania infantum* infections on animal health and welfare, human health, as well as its environmental impact in the regions of the EU where the disease is endemic.**
- **Efficacy of available preventive measures to protect dogs against *Leishmania infantum* infection, with the objective of mitigating the probability of introduction of the infection into free areas in the EU through movements of infected dogs.**
- **Probability that infection would become established in free areas of the EU if *Leishmania infantum* were introduced by infected dogs.**

EVIDENCE USED IN OPINION

- **Systematic reviews**
  - characteristics of CanL
  - preventative measures
  - diagnostics and treatment of CanL
- **Development of a stochastic model for assessing the probability of introduction and establishment**
  - parameterised based on systematic review and expert knowledge

LITERATURE REVIEW, SURVEY, MODEL

Preventive Veterinary Medicine

journal homepage: www.elsevier.com/locate/prevetmed

A systematic review of the efficacy of prophylactic control measures for naturally-occurring canine leishmaniosis, part I: Vaccinations

C.E. Wylie[a,*], M. Carbonell-Antoñanzas[a], E. Aiassa[b], S. Dhollander[b], F.J. Zagmutt[c], D.C. Brodbelt[d], L. Solano-Gallego[a]

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ABSTRACT

Canine leishmaniosis (CanL) is an important zoonotic disease; however, th
able vaccines for the prevention of naturally-occurring *Leishmania infan*
currently a
e 2011, U.S

The Veterinary Journal

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The frequency and distribution of canine leishmaniosis diagnosed by veterinary practitioners in Europe

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ABSTRACT

This study aimed to evaluate the frequency and spatial distribution of canine leishmanio
Greece, Italy, Portugal and Spain. An online questionnaire investigated the location and
cases diagnosed by veterinary practitioners. Further data from the practice managem
erinary clinics in France were provided by a financial benchmarking company in re
ment and test invoice data from participating practices. The geographical and tempo
leishmaniosis was explored using Google Trends.

Veterinary practitioners from France, Greece, Italy, Portugal and Spain complet
naires. The percentage of practice-attending dogs with a veterinary diagnosis of CanL
in France to 7.80% in Greece. However, due to regional differences in response rates, pa
the mean regional estimates may better reflect the disease burden. Benchmarking
proximately 180,000 dogs estimated that 0.05% of dogs attending veterinary clinics we

Preventive Veterinary Medicine

journal homepage: www.elsevier.com/locate/prevetmed

Review

A systematic review of the efficacy of prophylactic control measures for naturally occurring canine leishmaniosis. Part II: Topically applied insecticide treatments and prophylactic medications

C.E. Wylie[a,*], M. Carbonell-Antoñanzas[a], E. Aiassa[b], S. Dhollander[b], F.J. Zagmutt[c], D.C. Brodbelt[d,1], L. Solano-Gallego[a,1]

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Modelling canine leishmaniasis spread to non-endemic areas of Europe

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SUMMARY

Expansion of sandflies and increasing pet travel have raised concerns about canine leishmaniasis (CanL) spread to new areas of Europe. This study aimed to estimate the probability of CanL introduction and persistence following movements of infected dogs. Stochastic modelling was used to estimate the probabilities of (1) CanL infection during travels or imports of infected dogs (P_{inf} and P_{infCA}, respectively), (2) CanL persistence in a dog network with sandflies after introduction of an infected dog (P_{per}), and (3) persistence in a CanL-free region (P_{per_region}) for

CHARACTERISATION OF CANINE LEISHMANIOSIS

1. Epidemiology

- Geographical distribution of CanL in Europe
- Prevalence of CanL in Europe
- Geographic distribution of phlebotomine vectors
- Affected species
- Life cycle
- Modalities of transmission between mammals (vectorial and non-vectorial)
- Potential persistence of L. infantum

2. Impact of the disease and prevention measures on:

- Animal health and welfare
- Human health

EFFICACY MITIGATION INTRODUCTION INFECTED DOGS

1. Preventative interventions

- Vaccination
- Topical insecticides
- Prophylactic medication
- Effects of preventative measures on animal welfare

2. Performance of diagnostic tests and treatments

- Performance of the currently available diagnostic tests for detection of *L. infantum*
- Efficacy of available treatments for *L. infantum* infection in dogs

3. Evaluation of the efficacy of available preventative measures

- Vaccination
- Topical insecticides
- Combined use of vaccination and topically applied insecticide
- Test and exclusion prior to entering free areas

ESTABLISHMENT PROBABILITY INFECTED DOGS

1. **Introduction into free areas without competent vectors**

2. **Introduction into free areas with competent vectors**

Assessment Conclusions

CHARACTERISE CANINE LEISHMANIOSIS IN EUROPE

- CanL is endemic in the **European countries or regions surrounding the Mediterranean** where disease distribution matches that of the phlebotomine vectors.
- On average, around **10 %** of dogs in endemic countries are **seropositive** for *L. infantum*, with wide variations between territories.
- Studies conducted in endemic areas have given much higher prevalences than serology, with up to **80 %** of the dog population being **PCR-positive**.
- Infection in the canine population in endemic areas of Europe is widespread and the **prevalence of infection** in dogs is **much higher than the fraction that shows clinical illness or seroconversion**.

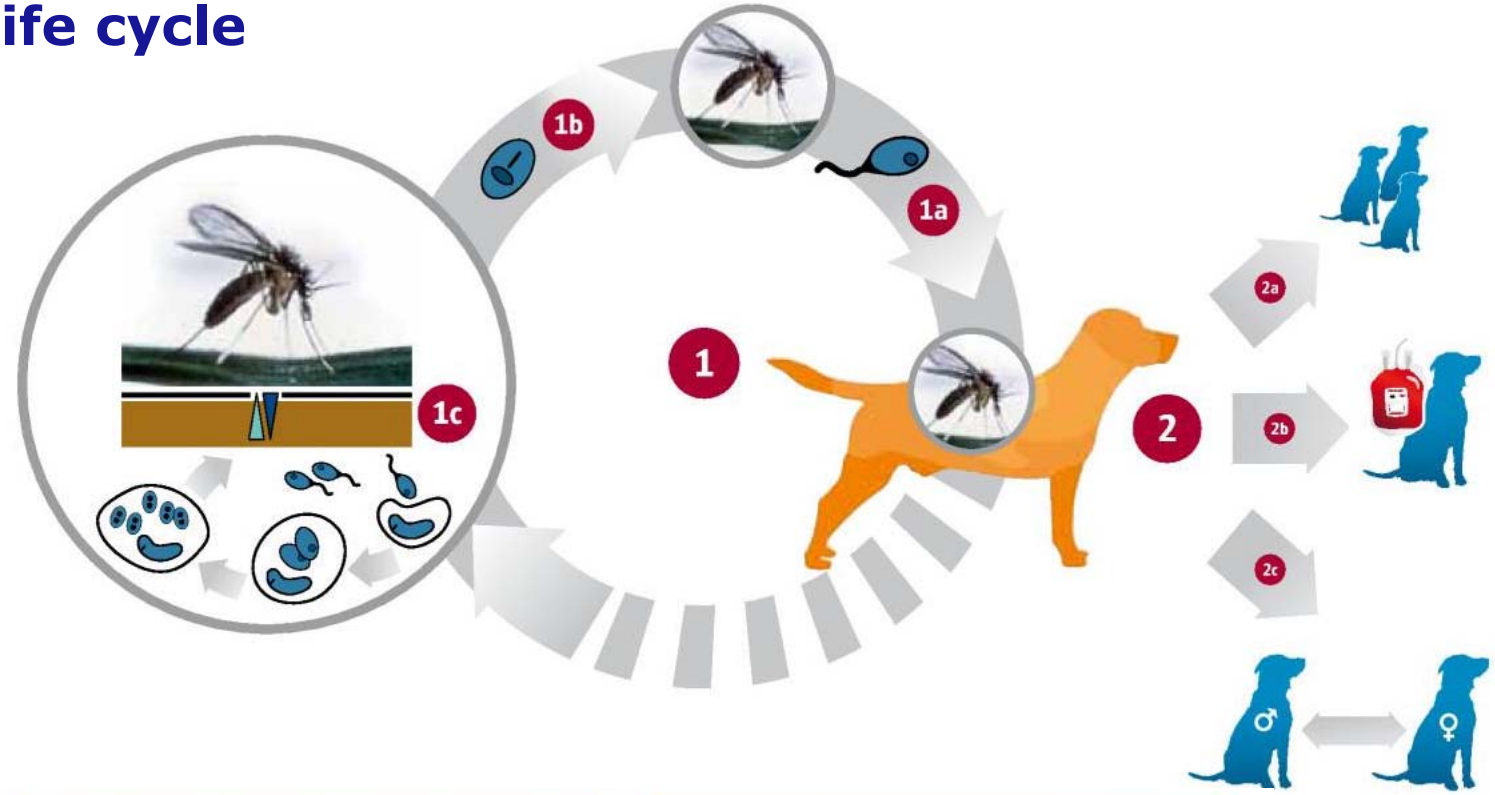
CHARACTERISE CANINE LEISHMANIOSIS IN EUROPE

- **Limited knowledge** in **central European** countries about **presence** of competent vectors and presence of endemic CanL.

- **Data on sandflies** are **limited** because of the absence of systematic sampling programmes and expertise.
- Available field data suggest that **sandflies are spreading northwards** in Europe and their **densities are increasing** in some newly colonised areas.
- Once infected, a **sandfly** remains **infected for life**, that is, on average, two to three weeks. Vertical transmission of Leishmania has not been reported in sandflies.

CHARACTERISE CANINE LEISHMANIOSIS IN EUROPE

Life cycle



1. Classical life cycle of *Leishmania infantum*
   - 1a. Promastigote
   - 1b. Amastigote
   - 1c. Parasite dissemination to organs in macrophages

2. Other unusual modes of transmission
   - 2a. Vertical
   - 2b. Blood transfusion
   - 2c. Venereal transmission

   Other (unproven): Dog to dog (bites, wounds)

Source: http://www.parasitesandvectors.com/content/4/1/86

CHARACTERISE CANINE LEISHMANIOSIS IN EUROPE

- **No CanL endemic situation** has been observed **in areas without competent vectors**, suggesting that none of the transmission routes appears to sustain infection in a large population (i.e. larger than that of a household or a kennel).

- In northern European countries, where competent vectors have not been found, "imported" cases in dogs with a history of travelling from endemic areas and **CanL foci in households or in kennels** have been described. These foci can last for several years because of **non-vectorial transmission**.

CHARACTERISE CANINE LEISHMANIOSIS IN EUROPE

- Infection **spreads quickly** and **extensively** among the dog population in **optimal environmental conditions** (vectors, contacts).
- **All seropositive** *L. infantum*-infected dogs, whether they express clinical disease or not, are **potential sources** of infection for vectors and may transmit the parasite.
- Role of wild mammals as reservoirs not fully demonstrated. **Black rats**, **wild rabbits** and **hares** may contribute to **maintaining** *L. infantum* circulation in some areas of southern Europe.
- **Impact** of *L. infantum* infection on dog health/ welfare depends on **severity**, which ranges from subclinical to very severe, including euthanasia.

CHARACTERISE CANINE LEISHMANIOSIS IN EUROPE

Humans:

- Average incidence of **visceral leishmaniosis** reported in humans in southern Europe **2-134 cases** per year / country
- Average incidence of **cutaneous form** reported in humans in southern Europe **1-50 cases** per year / country.
- **Most** human *L. infantum* infections **asymptomatic**.
- Risk factors for clinical disease: young age, HIV infection, other i**mmuno-suppressive** states.

EFFICACY MITIGATION INTRODUCTION INFECTED DOGS

- **Vaccine**: no full protection against infection or disease. Some vaccines, e.g. CaniLeish®, the only vaccine authorised in the EU, provide **partial protection** against active *L. infantum* infection and clinical disease in dogs.

- **Topically applied insecticides**: demonstrated mass treatment efficacy, efficacy of insecticides in individual dogs when application is their owners' responsibility **uncertain**.

EFFICACY MITIGATION INTRODUCTION INFECTED DOGS

- **Prophylactic medication** with domperidone: **limited data** on efficacy in endemic areas, data on treatments of immunologically naive dogs and its potential long-term toxicity are lacking.

- **Drug therapy**: appears to mainly **slow down** the progression of infection, **decrease infectiousness** and **improve clinical manifestations** by reducing parasite loads in infected tissues, but no treatment (drugs and regime) tested so far has demonstrated 100 % efficacy in the elimination of the parasites.

ESTABLISHMENT PROBABILITY INFECTED DOGS

- Owing to the limited available knowledge on factors such as vector competence and abundance, dog distribution and movements, the average **probability** of **introduction** and **establishment** of CanL in a **theoretical dog network** or a network of networks was **estimated**, assuming the presence of competent vectors in some areas in a CanL-free area.
- The model assessed the average probability of disease establishment, defined as the **local transmission of from vector to host and vice versa**, leading to the temporal presence of at least one indigenous infectious host and at least one

ESTABLISHMENT PROBABILITY INFECTED DOGS

- Even in areas where sandfly populations are likely to have a **lower vectorial capacity than in endemic** areas, e.g. in some foci with low vector densities, the average probability of establishment following introduction of an infected dog remains **high**, according to the model.
- Although the average probability of establishment in a non-endemic region with competent sandflies may be very high, according to the model, the **prevalence** in that region in the event of CanL introduction and establishment may vary from **extremely low to high**, depending mainly on the **vectorial capacity**.

ESTABLISHMENT PROBABILITY INFECTED DOGS

- Owing to the wide distribution of susceptible dogs and the high host–vector contact rates, the main **limitation** to CanL **spread** is represented by the vectors. This reinforces the **need for knowledge** of the **vectorial competence** of some sandfly species and of the **distribution and abundance** of known vectors.
- Results from the model indicated that the **probability** of introduction and establishment can be **reduced by mitigation measures**, separately or in combination. The **most effective** mitigation measure to reduce the probability of introduction and establishment of CanL was **topically applied**

ESTABLISHMENT PROBABILITY INFECTED DOGS

- The model indicated that **vaccination** of dogs **prior** to travelling to endemic areas had only a **limited effect** on the probability of establishment in a non-endemic region, and this effect seems more apparent when the vectorial capacity and the number of introduced dogs were low.
- The use of **topical insecticide and vaccination** in travelling dogs had a **synergistic** effect in reducing the probability of establishment in a dog network and in reducing the probability of establishment in a region after their return to a non-endemic area, according to the model. Again, this effect was more marked in areas where a low

ESTABLISHMENT PROBABILITY INFECTED DOGS

- **Testing** dogs **before** their introduction into a **non-endemic** area is of limited value if applied shortly after exposure to infected sandflies. This is mainly because of it takes several months after exposure before testing gives a positive result.
- **Test and treatment** in the **endemic** area, prior to movement into a non-endemic area, will reduce disease risk in individual animals; however, it does **not** appear to be an **efficient** and realistic option to **mitigate the risk of introduction** of CanL into the non-endemic area, as no treatment against *L. infantum* infection can provide permanent parasitological cure.

Recommendations

RECOMMENDATIONS FOR PREVENTING INTRODUCTION

- **Owners** of dogs travelling from free areas to endemic areas should be **informed about the risks** posed by CanL and **potential risk mitigation measures**.
- The most useful **diagnostic approaches** for investigation of infection in sick and clinically healthy infected dogs include (1) detection of specific anti-leishmanial antibodies in serum using **quantitative serological techniques** and (2) demonstration of **parasite DNA in tissues** by applying molecular techniques. To optimise the sensitivity of CanL diagnostics, especially in subclinical dogs, the two techniques should be **used in parallel**.
- Dogs born in endemic areas, which are confirmed to be infected with *L. infantum* by an appropriate test, should

RECOMMENDATIONS FOR PREVENTING INTRODUCTION

- To prevent CanL introduction and establishment in non-endemic areas via measures imposed on dogs travelling to and from or imported from endemic areas, the use **topical insecticides** is strongly recommended.
- Exclusion of **travelling dogs testing positive** by means of serology and/or PCR after their return may not be imposed on dog owners. However, the **close clinical monitoring** of these dogs is recommended, including **medical treatment**, which will mitigate the risk of disease and its impact on welfare, and which will reduce parasite loads and infectiousness of the dog.
- In addition, when the **presence of competent vectors** in a free area is known, the use of **insecticide collars in**

RECOMMENDATIONS FOR FURTHER RESEARCH

- Well-designed, adequately powered **RCTs** on the **efficacy** of the **preventative measures**, such as vaccination and application of topical insecticides, alone and in combination, should be carried out.

- **Sensitivity** and **specificity** of **diagnostic tests** for detecting *L. infantum* should be quantified, e.g. by latent class analysis, using two different test principles (serology and PCR).

- **Diagnostics** and **prognostic tests** in dogs should be improved and developed, e.g. biomarkers to differentiate **status of infection and infectiousness** should be developed.

THANK YOU FOR YOUR ATTENTION