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Afonso, P; Cardoso, L; Soares, AS; Matos, M; Quintas, H; Coelho, AC.

Corresponding author:
Paulo Afonso

afonso@ipb.pt

Affiliations:
1 CECAV – Animal and Veterinary Research Centre, University of Trás-os-Montes e Alto Douro (UTAD), Vila Real, Portugal
2 Associate Laboratory for Animal and Veterinary Sciences (AL4AnimalS), Portugal
3 Centro de Investigação de Montanha (CIMO), Instituto Politécnico de Bragança, Campus de Santa Apolónia, 5300-253, Bragança, Portugal
4 Laboratório Associado para a Sustentabilidade e Tecnologia em Regiões de Montanha (LASus-TEC), Instituto Politécnico de Bragança, Campus de Santa Apolónia, 5300-253, Bragança, Portugal.

ADMINISTRATIVE INFORMATION

Support - This study was supported by projects UIDB/CVT/00772/2020 and LA/P/0059/2020, funded by the Portuguese Foundation for Science and Technology (FCT).

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202480010

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 02 August 2024 and was last updated on 06 May 2025.

INTRODUCTION

Review question / Objective Identify the best available evidence regarding the epidemic, clinical features, and the prevalence of *T. marneffeii* reported in companion animals, wildlife, and humans in Europe.

Condition being studied Talaromycosis (infection by *Talaromyces marneffeii*) in European humans, companion animals and wildlife.

METHODS

Search strategy The initial literature search was conducted between February and 6 September 2022. To ensure the review remains up to date, the

same search strategy and eligibility criteria were reapplied in April 2025, covering the period up to 30 April 2025. No additional eligible studies were identified in this updated search.

Participant or population Patient.

Intervention Not applicable.

Comparator Not applicable.

Study designs to be included Case reports or cross-sectional studies describing clinical and epidemiological characteristics or where the prevalence of infection/disease could be calculated from available data were included in this current study according to PRISMA guidelines.

Eligibility criteria Case reports or cross-sectional studies describing clinical and epidemiological characteristics or where the prevalence of infection/disease could be calculated from available data were included in this current study according to PRISMA guidelines.

Short communications and case reports addressing: (i) information on the clinical presentation of talaromycosis by *T. marneffei* in animals and humans; and (ii) the prevalence of the disease in animals and humans were included. Review articles, case-control studies, conference proceedings, and book chapters were excluded. Research notes, editorials, experimental assays, proceedings, articles without primary data, and dissertations/theses with unpublished data were also excluded.

Information sources Articles were retrieved from the PubMed, ScienceDirect and Web of Science databases. Search terms included a combination of Europe AND (*Talaromyces marneffei* OR Talaromycosis OR *Penicillium marneffei* OR penicilliosis). Refer-ences from publications obtained were also checked to identify additional papers suitable under the inclusion criteria. The search was not restricted by language or year. Studies published until 05 September 2022 were included.

The searches were performed between February and September 2022. However, due to the few publications reporting *T. marneffei*, talaromycosis, *P. marneffei*, or penicilliosis in animals, the geographic scope was extended worldwide.

Main outcome(s) Prevalence of *Talaromyces marneffei* Infections:

In humans, companion animals, and wildlife in Europe.

Timing: Data included studies published up to 5 September 2022.

Clinical Features:

Detailed clinical presentations of talaromycosis in reported cases.

Common symptoms: fever, weight loss, cough, skin lesions, lymphadenopathy, hepato-splenomegaly, anemia, and weakness.

Epidemiological Characteristics:

Geographic distribution of reported cases within Europe.

Demographic details: age, sex, immuno-compromised status (e.g., HIV-positive).

Diagnosis and Misdiagnosis:

Methods used for diagnosis: microscopy, culture, histopathology, and molecular techniques.

Instances of misdiagnosis due to non-specific symptoms.

Treatment and Outcomes:

Antifungal therapies used: Amphotericin B, Itraconazole, Voriconazole.

Patient outcomes based on the timing of diagnosis and treatment effectiveness.

Effect Measures:

Frequency and Distribution:

Number of cases reported by country and year.

Percentage of cases in HIV-positive vs. HIV-negative patients.

Clinical Presentation Statistics:

Proportion of cases exhibiting specific symptoms (e.g., 96.3% had fever, 63.0% had skin lesions).

Diagnosis Timeliness:

Impact of early vs. late diagnosis on patient outcomes.

Measures: time to diagnosis, time to initiation of treatment.

Treatment Efficacy:

Success rates of different antifungal treatments.

Measures: response to treatment, recurrence rates, mortality rates.

Relevant Details:

Human Cases: 29 cases reported in 11 European countries over different decades.

Animal Cases: Reports in dogs, an Egyptian mongoose, and a *Cynomolgus* macaque.

Geographical Spread: Cases identified in Belgium, Denmark, France, Germany, Greece, Italy, Netherlands, Spain, Sweden, Switzerland, and the United Kingdom.

Quality assessment / Risk of bias analysis The studies included in this review comprised case reports, cross-sectional studies, short communications, clinical studies, and observational studies. Data from each study were extracted using a standardized form. Two independent reviewers assessed the quality and risk of bias for each study. Discrepancies between reviewers were resolved through discussion or by consulting a third reviewer to reach a consensus.

Strategy of data synthesis Screening and data extraction

Two independent reviewers selected publications based on their titles or abstracts. Duplicate records were excluded using a bibliographic manager tool (Mendeley® Reference Manager version 2.70.0). Those publications meeting the inclusion criteria and those with titles and/or abstracts doubtful to exclude were fully read. Any different opinion was discussed, and a consensus position was agreed upon.

Two authors compiled data on an electronic spreadsheet in three groups: (i) companion animals; (ii) wildlife; and (iii) humans.

Equivalent information was extracted from all included studies. This qualitative information

includes information on the country, authors, and year of publication and about species, breed, age, gender, geography, lifestyle, number of infected animals, and clinical features.

Data analysis

Data were analysed with JMP® Statistical Discovery Version 16.2.0.

Subgroup analysis Not applicable.

Sensitivity analysis Not applicable.

Language restriction Not applicable.

Country(ies) involved Portugal.

Keywords Animals, Europe, Humans, Planetary Health, Stockholm paradigm, Talaromyces marneffeii.

Contributions of each author

Author 1 - Paulo Afonso - Conceptualisation, Data curation and Formal Analysis; Funding acquisition; Investigation; Methodology: PA; Visualization: PA; Writing – original draft; Writing – review & editing.

Email: afonso@ipb.pt

Author 2 - Luís Cardoso - Conceptualisation, Data curation and Formal Analysis; Methodology; Supervision; Visualization; Writing – review & editing.

Email: lcardoso@utad.pt

Author 3 - Ana Sofia Soares - Visualization; Writing – review & editing.

Email: anasoares@utad.pt

Author 4 - Manuela Matos - Visualization; Writing – review & editing.

Email: mmatos@utad.pt

Author 5 - Hélder Quintas - Conceptualisation, Data curation and Formal Analysis; Methodology; Supervision; Visualization; Writing – review & editing.

Email: helder5tas@ipb.pt

Author 6 - Ana Cláudia Coelho - Conceptualisation, Data curation and Formal Analysis; Methodology; Supervision; Visualization; Writing – original draft; Writing – review & editing.

Email: accoelho@utad.pt