Spatial patterns of classical scrapie in small ruminants and Creutzfeldt-Jakob disease in humans: a geographical approach to investigate the zoonotic potential of scrapie

Rosanna Desiato[1], Allegra Sartore[2], Paola Barzanti[1], Mattia Begovoeva[1], Anna Ladogana[3], Maria Puopolo[3], Dorina Tiple[3], Luana Vaianella[3], Elisa Colaizzo[3], Dolores Catelan[2], Giuseppe Ru[1]

[1]Istituto Zooprofilattico Sperimentale del Piemonte, Liguria e Valle d'Aosta, European Union Reference Laboratory (EURL) for Transmissible Spongiform Encephalopathies (TSEs), Turin, Italy; [2]Unit of Biostatistics, Epidemiology and Public Health, Department of Cardiac, Thoracic, Vascular Sciences and Public Health University of Padua, Padua, Italy; [3] Istituto Superiore di Sanità, National Registry of Creutzfeldt-Jakob disease (CJD) and related disorders, Rome, Italy

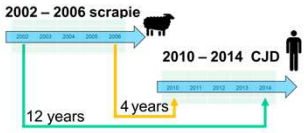
Introduction

Classical scrapie (CS) is a transmissible spongiform encephalopathy with a hypothesized, but unconfirmed, zoonotic potential. This study investigated that potential by comparing the geographical distribution of CS in Italy with that of Creutzfeldt-Jakob disease (CJD).

Material & methods

Accounting for a latency period, data from 135 CS outbreaks identified through testing 31,552 herds (01/01/2002 - 31/12/2006) and 506 CJD deaths (01/01/2010 – 31/12/2014) were analysed. Standardized mortality ratios (SMRs) were calculated at provincial level, adjusted for flock-level surveillance intensity (CS) and age and sex (CJD).

A latency period of 4 to 12 years was considered as a plausible latency period for CJD after exposure to CS.



Geographical patterns were assessed using Bayesian Poisson-Gamma and Besag-York and Mollié (BYM) models separately for each disease. Bayesian shared components models were used to identify areas with common spatial risk. Finally, an ecological regression model was used to assess the association between CJD (outcome) and CS (exposure).

Results

The maps (Figures 1A and 1B) show that the distribution of SMRs for both CJD and scrapie is highly heterogeneous, with areas of excess risk not only in Sardinia and Sicily, but also in central Italy and, for CJD only, in north-eastern Italy.

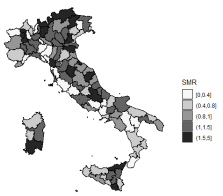


Fig 1A: SMRs of **CJD** in 2010-2014.

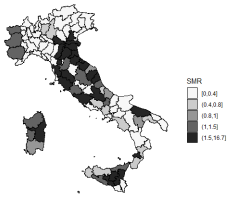


Fig. 1B: SMRs of **scrapie** in 2002-2006.

Both Poisson-Gamma (Figures 2A and 2B) and BYM models (Figures 3A and 3B) revealed spatial heterogeneity for CS and CJD, highlighting high-risk areas in Sicily, Sardinia and central Italy.

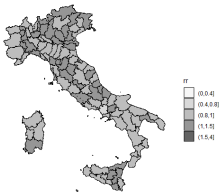


Fig 2A: RRs (relative risk) of **CJD** in the period 2010-2014 on absolute scale.

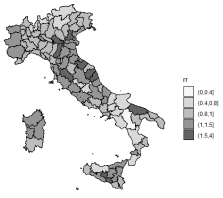


Fig 2B: RRs (relative risk) of **scrapie** in the period 2002-2006 on absolute scale.

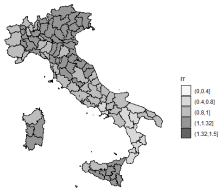


Fig. 3A. RRs (relative risk) of **CJD** in the period 2010-2014 on absolute scale.

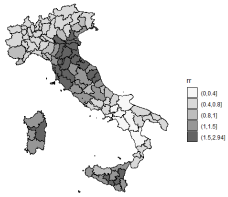


Fig 3B: RRs (relative risk) of **scrapie** in the period 2002-2006 on absolute scale.

The Bayesian shared component model suggested the presence of areas with latent risk factors common to both diseases (Figures 4A and 4B).

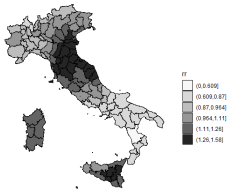


Fig 4A: shared risk of shared component analysis on relative scale.

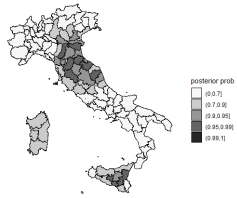


Fig 4B: posterior probability of shared component analysis (shared RR > 1) on absolute scale.

The ecological regression model indicated a weak but positive association between the distribution of CS and CJD (β=0.02; 95% CrI: -0.0105 -0.05581), with a distribution of beta spatially structured showed in Figures 5A and 5B.

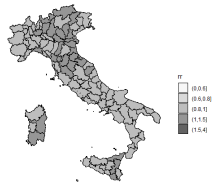


Fig 5A: **CJD** risk (beta spatially structured - no clustering) in the period 2010-2014.

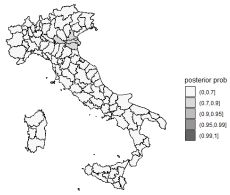


Fig 5B: **CJD** posterior probability (RR>1) (no clustering).

Conclusions

In conclusion, the consistency of findings across multiple Bayesian models supports the hypothesis of overlapping spatial risk factors for CS and CJD. Although the ecological association was weak and the study design is inherently weaker than cohort or case-control studies which gather data at the individual level, the result of this work align with the hypothesis of the zoonotic potential of scrapie.