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A systematic review on the prevalence of tick-borne encephalitis infection in milk and milk products in Europe

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Introduction

Tick-borne encephalitis virus (TBEv) is a Flavivirus responsible for one of the most important zoonoses in Europe, whose incidence increasing. Although tick-borne encephalitis (TBE) is a vector-borne disease and is mainly transmitted to humans through the bite of infected ticks, it can also be contracted through the consumption of raw milk and dairy products from viremic domestic ruminants (1 We conducted a systematic review to assess the prevalence of TBEv in milk and milk products from domestic ruminants in Europe, an to evaluate the usefulness of monitoring TBEv infection in dairy products for the early identification of the viral circulation in geographic area.

Materials and methods

Following protocol registration (PROSPERO: CRD 42021279317), a comprehensive search was performed in three databases (Medline EMBASE and CAB Abstracts) to identify relevant studies published from Jan 1980-Nov 2022. Screening, data extraction and critica appraisal (2) were conducted independently by two reviewers. Meta-analysis of prevalence were estimated using random effects Separate meta-analyses were conducted based on type of sample collected (individual milk, bulk milk, cheese). Where possible subgroup analyses were performed by animal species.

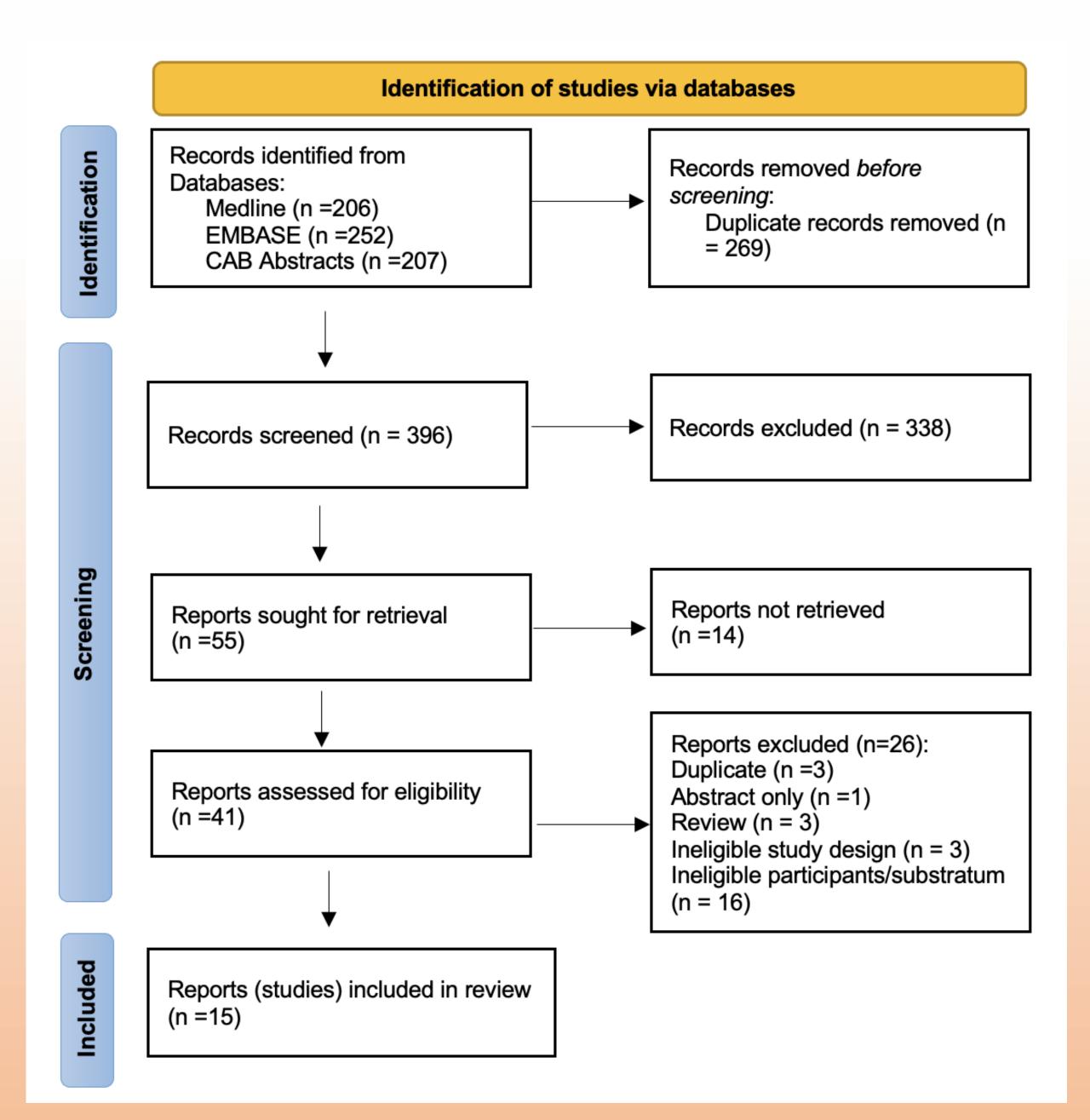


Fig.1 PRISMA Flow chart

References: (1) ECDC, 2022: https://www.ecdc.europa.eu/en/tick-borne-encephalitis/facts/factsheet; (2) JBI Critical Appraisal Tool: https://jbi.global/critical-appraisaltools (3) Pautienius et al. Bulk Milk Tank Samples Are Suitable to Assess Circulation of Tick-Borne Encephalitis Virus in High Endemic Areas. Viruses. 2021; (4) Imhoff et al., Review: Sentinels of tick-borne encephalitis risk. Ticks Tick Borne Dis. 2015; (5) Bormane et al. Vectors of tick-borne diseases and epidemiological situation in Latvia in 1993-2002. Int J Med Microbiol. 2004

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A systematic review on the prevalence of tick-borne encephalitis infection in milk and milk products in Europe



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Study	ES (95% CI)	% Weig
Cow		
Caini2012 (November, Hungary)	0.00 (0.00, 0.28)	5.27
Cisak2010 (July, Poland)	0.11 (0.05, 0.21)	12.65
Paulsen2019 (October, Norway)	0.29 (0.08, 0.64)	4.12
Paulsen2019 (June, Norway)	0.14 (0.05, 0.33)	8.40
Paulsen2019 (November, Norway)	0.00 (0.00, 0.17)	7.78
Paulsen2019 (October, Norway)	0.00 (0.00, 0.18)	7.31
Paulsen2019 (March-September, Norway)	0.02 (0.00, 0.11)	11.57
Subtotal (I^2 = 49.96%, p = 0.06)	0.04 (0.00, 0.11)	57.10
Goat		
Cisak2010 (June, Poland)	0.21 (0.10, 0.38)	9.58
Gonzalez2022 (October, France)	0.05 (0.02, 0.15)	12.16
Holzmann2009 (October, Austria)	0.00 (0.00, 0.79)	1.01
Hudopisk2013 (September, Slovenia)	0.25 (0.05, 0.70)	2.73
Ilic2020 (September, Croatia)	0.00 (0.00, 0.24)	5.93
Khol1996 (July, Slovakia)	0.00 (0.00, 0.56)	2.20
Subtotal (I^2 = 29.04%, p = 0.22)	0.03 (0.00, 0.13)	33.62
Sheep		
Cisak2010 (July, Poland)	0.22 (0.11, 0.41)	9.28
Heterogeneity between groups: p = 0.088		
· · · · · · · · · · · · · · · · · · ·	0.04 (0.00, 0.10)	100.0
Overall (I^2 = 47.26%, p = 0.03);	0.04 (0.00, 0.10)	10

Fig.2 Pooled prevalence of TBEv in individual samples of raw milk

of	Study	ES (95% CI)
).		
· .	Cow	
d	Gonzalez2022 (June, France, n=1)	0.00 (0.00, 0.79)
a	Paulsen2019 (October, Norway, n=2)	1.00 (0.34, 1.00)
	Paulsen2019 (September, Norway, n=1)	0.00 (0.00, 0.79)
	Paulsen2019 (June, Norway, n=1)	0.00 (0.00, 0.79)
	Paulsen2019 (September, Norway, n=1)	0.00 (0.00, 0.79)
e,	Goat	
·	Brockmann2018 (June, Germany, n=1)	0.00 (0.00, 0.79)
al	Gonzalez2022 (June, France, n=1)	1.00 (0.21, 1.00)
S.	Milonaki2022 (June-September, Austria, n=1)	1.00 (0.21, 1.00)
e,	Pautienius2021 (April-November, Lithuania, n=1363)	0.04 (0.03, 0.05)
	Sheep	
	Paralikova2022 (March-September, Slovakia, n=2)	0.00 (0.00, 0.66)
	Pautienius2021 (April-November, Lithuania, n=312)	0.04 (0.03, 0.07)
	1234	5.6.7.8.91
	Proportion	.5.0.7.0.91

Fig.3 Pooled prevalence of TBEv in bulk milk tank samples of raw milk

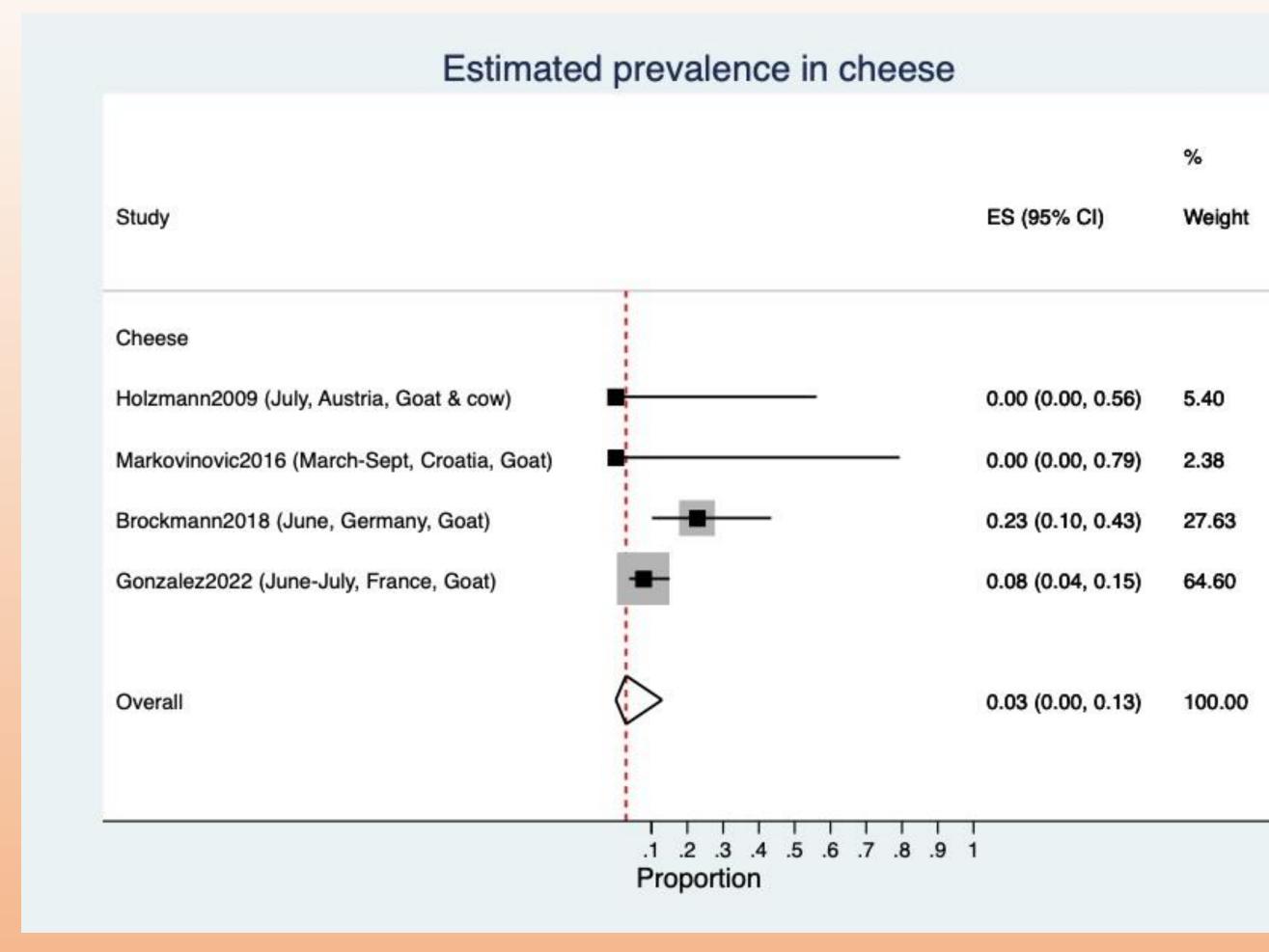
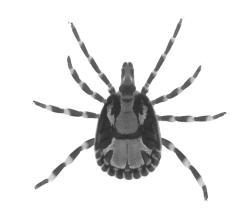


Fig.4 Prevalence estimates of TBEv in cheese made from raw milk









Results

Fifteen studies were included in the review (Fig.1), ten of which were outbreak investigations, following TBE cases in humans, and 5 were surveys. Goat products were analysed in 10 studies, cow in 6, and sheep in 4. 29 prevalence estimates used direct diagnostic (PCR & VNT) and 6 used indirect diagnostic (ELISA). The sample size used for estimating prevalence ranged from 1-1363 samples.

The pooled prevalence of TBEv in individual raw milk samples was 4% (95% CI 0-10%; Fig.2), with similar findings for cow milk (4%, 95% CI 0-11%) and goat milk (3%, 95% CI 0-13%); however, the prevalence was 22% (95% CI 11-41%) in the one study in sheep milk. The prevalence estimates for TBEv in bulk milk tanks were too heterogeneous, with most values either 0% or 100% in studies with sample sizes of one or two, therefore metaanalysis was not conducted (Fig.3). The pooled prevalence of TBEv in cheese made from raw milk was 3% (95% CI 0-13%; Fig.4).

Discussion

Epidemiological surveillance of TBEv in field ticks and wild vertebrate hosts can be challenging, due the focal nature of TBEv occurrence, to the specific expertise required and limits in laboratory tests (3). Our systematic review shows that a variable prevalence of TBEv in milk products can be found (3-22%) as well as in ticks (0.1-37.3%) (4, 5). However, surveillance on milk and milk products from grazing domestic ruminants can be a valuable tool for studying TBEv prevalence and assessing the epidemiological situation in a geographic area. Dairy products can be easily obtained and their testing can be helpful for risk assessment and for the epidemiological surveillance of TBE in a One Health perspective.