

TBE in Italy

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E-CDC risk status: endemic (last edited: date 19/03/2024, data from 2023)

History and current situation

Italy is considered a low-incidence country for tick-borne encephalitis (TBE) in Europe¹. Areas at higher risk for TBE within Italy are geographically clustered in the forested and mountainous regions and provinces of the northeastern part of the country, as suggested by TBE case series published over the last decade²⁻⁴. A national enhanced surveillance system for TBE has been established since 2017⁵. Before this, information on the occurrence of TBE cases at the national level in Italy was lacking. Both incidence rates and the geographical distribution of the disease were mostly inferred from endemic areas where surveillance was already in place, and from ad hoc studies and international literature. TBE has been recorded in Italy since 1967, with foci of infections in the northeast (Trento, Belluno and Gorizia) and central (Florence and Latina) provinces⁶⁻⁹. TBE presence in central Italy has not been confirmed by further studies on ticks and serosurveys conducted afterwards^{10,11}, nor by human cases, posing concerns about possible misdiagnosis.

Serological investigations of people at risk, such as forestry rangers, hunters, hikers and forest products collectors, have been performed in order to get information on human exposure to TBE virus (TBEV). Circulation in the pre-alpine and alpine regions reported partially NT-confirmed seroprevalence values of 0.6%, 1.07% and 3.2% in Friuli-Venezia Giulia¹², Trento province¹³ and Turin province¹⁴, respectively. Interestingly, Turin province has never reported TBE human cases, so far. A retrospective study conducted in 2015 in the northeast regions using the ECDC case definition of TBE³, allowed the identification of 367 cases (0.38 per 100,000 inhabitants) during the period from 2000 to 2013³. TBE cases were mainly males (70%) and the majority of them were between 30 and 70 years of age (see also [Figure 2](#)). A significant increase in the annual incidence rate (IR) was observed during the study period, from 0.18 per 100,000 in the year 2000 up to 0.59 per 100,000 in 2013 (95% confidence interval [CI]: 1.02–1.08, $P > 0.01$)³. The majority of TBE cases occurred between April and October, consistent with the seasonal activity of ticks. According to this study, the risk of TBE is associated with altitude, with the highest values found for municipalities between 400 and 600 m a.s.l., and the IR falling along with municipality

altitude decrease or increase³. In 2022, TBE showed a record in the number of cases and mortality rates, with 72 cases, mainly from four northeastern Italian regions and provinces¹⁵: Trento (18 cases), Friuli-Venezia Giulia (12 cases) and Veneto (37 cases), and sporadically from other locations i.e. Emilia Romagna (2 cases), Liguria (2 cases) and Lazio (1 case) ([Fig. 3](#)) and 3 fatal events, resulting in an exceptionally high mortality rate of 4.17%.

In its natural enzootic cycle, TBEV transmission involves ixodid ticks, mainly belonging to the genus *Ixodes*, and the small mammal hosts (rodents and insectivores) which support both ticks population and TBEV circulation. The link between tree masting, rodent population dynamics, density of nymphal ticks and eventually the incidence of tick-borne diseases in humans, has been investigated in several studies highlighting the expected two-year lag between a masting event and the increase in (infected) nymphs^{16,17}. In this context, a long-term study conducted in the Province of Trento positively correlated pollen data and TBE incidence in humans¹⁸, therefore offering to public health agencies a potential early warning tool that might be used to plan preventive measures two years in advance. Of note is the fact that a huge mast event involving two important forest species (*Fagus sylvatica* and *Picea abies*) was recorded in 2020 and that the peak in the number of TBE cases happened in 2022.

In particular, the province of Trento showed a sharp increase in TBE incidence since 2012, despite vaccination efforts. To assess the current risk of infection in the provincial territory, an integrated One-Health research approach was applied, combining the analysis of the distribution of human cases, the study of seroprevalence in sentinel hosts (goats) and the direct screening of questing ticks¹⁹. A total of 1.56% of goats resulted positive for specific antibodies for TBEV. Sampling of ticks was concentrated in areas where TBEV circulation was observed both in seropositive goats or in humans, resulting in a prevalence of 0.17%. In particular these results revealed an increased prevalence of TBEV in ticks and the emergence of new active TBE foci which are located northward and at higher altitude (1.109 m a.s.l.) compared to previous investigations. None of the areas with seropositive goats was confirmed by TBEV detection in ticks and recent human

cases, but this aspect needs further confirmation.

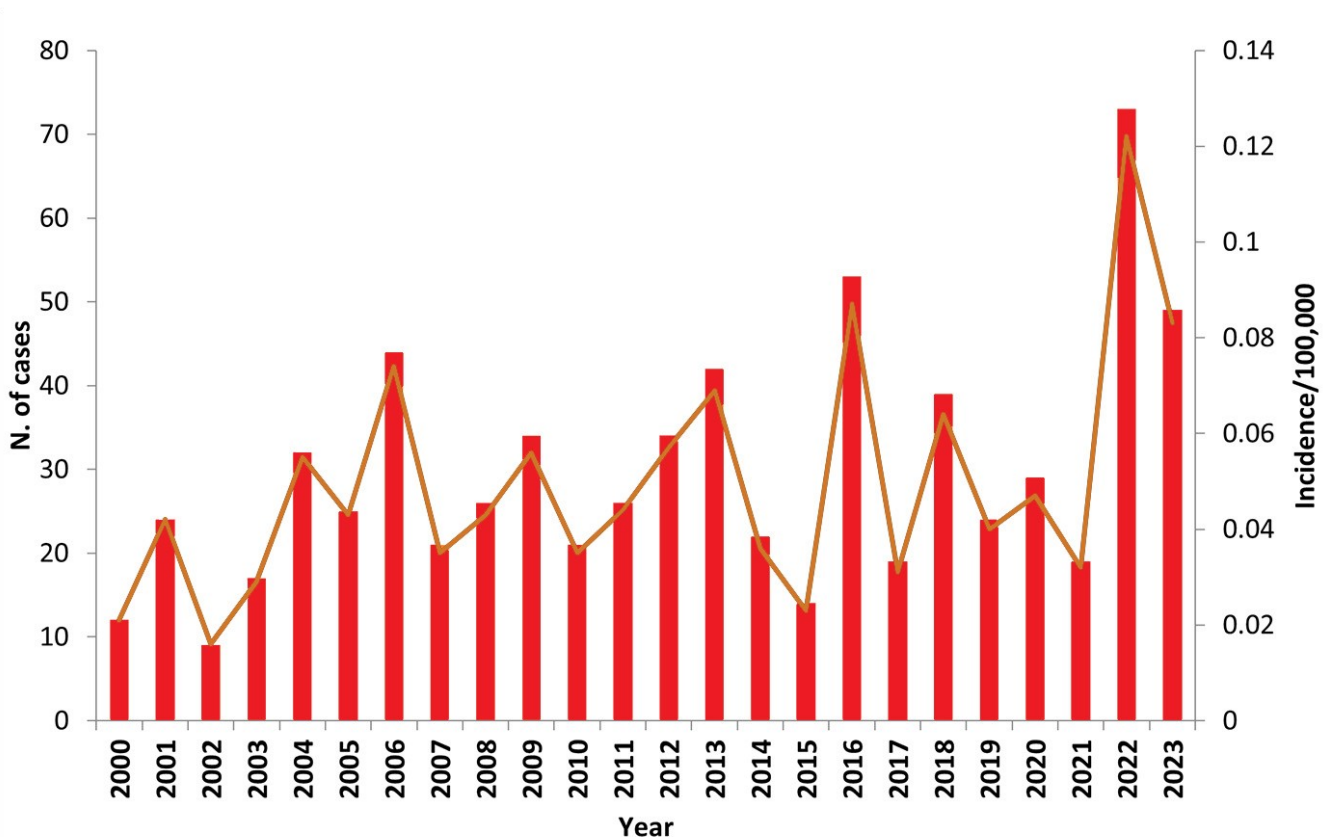
Since the 1990s, rising cervid population numbers and changes in forest structure in the northeastern regions and provinces of Italy were observed in conjunction with an increase in TBE incidence²⁰, but this relationship is not always positive and at a threshold density level of ungulates, TBEV prevalence decreases²¹. Transmission of TBEV from infected nymphs to co-feeding uninfected ticks on rodents is considered the most efficient route for the amplification of this virus, therefore, studies regarding the ecological and abiotic conditions affecting tick feeding dynamics are important. Recently a long-term longitudinal field study highlighted that the autumnal cooling rate and the presence of roe deer and mice are crucial ecological drivers for co-feeding transmission which in turn is reflected in the maintenance of a TBEV hotspot²². The animal community composition and abundance are known to affect transmission of tick-borne diseases, suggesting that in highly diverse habitats TBE risk decreases. Using habitat richness as a proxy for vertebrate host diversity, high TBE risk corresponded to areas with intermediate richness. In endemic areas, such as those located in northeast Italy, TBE risk is higher probably because it features habitat types that

are generally suitable for both ticks and hosts presence²³.

Vaccination for TBE is currently recommended in Italy among residents and occupationally exposed groups, living in rural endemic areas, but its impact on disease occurrence in the affected communities is not yet evaluated²⁴. In the Friuli-Venezia Giulia region since 2013 and in the Autonomous Provinces of Trento and Bolzano since 2018, TBE vaccine is offered free of charge to the resident population.

In conclusion, the incidence of TBE in Italy is relatively low and the risk appears to be geographically restricted to the pre-alpine and alpine regions of the country. However, recent increase and spread in the number of cases (see Figure 3), pose concerns regarding the importance of disentangling the complex factors that are involved in the spread and maintenance of TBEV in an endemic focus and the early-warning predictors that should be identified.

Figure 1: Reported human cases and incidence of TBE, Italy, 2000-2023.
Data on vaccine uptake not available.

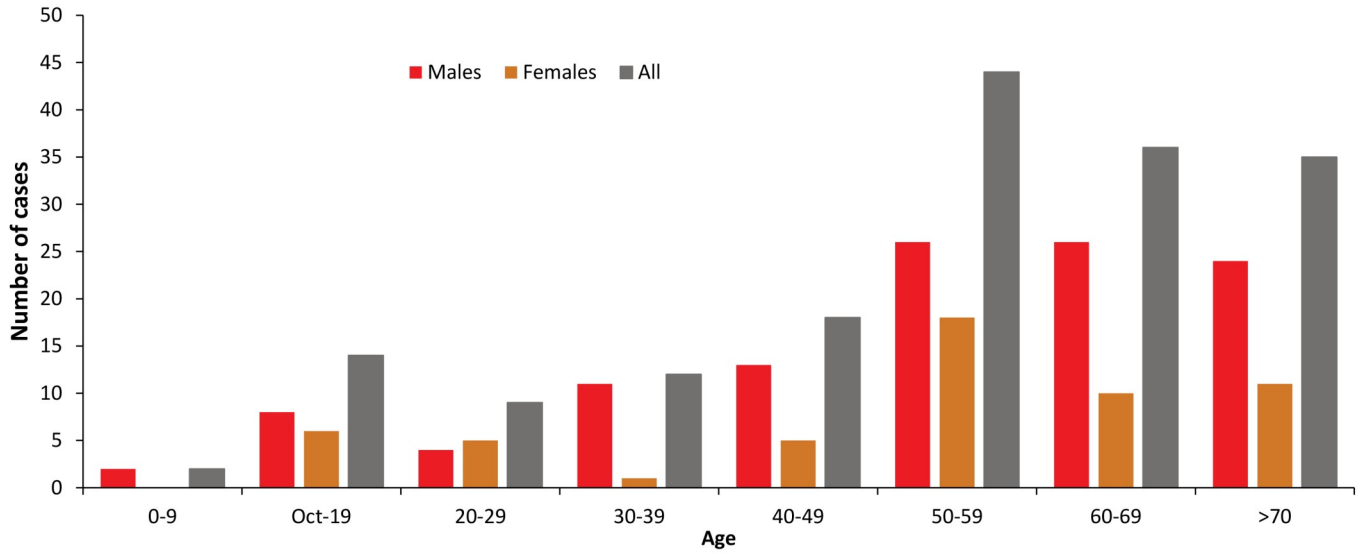


*Data on vaccination rate : Appendix—Figure 1

Overview of TBE in Italy

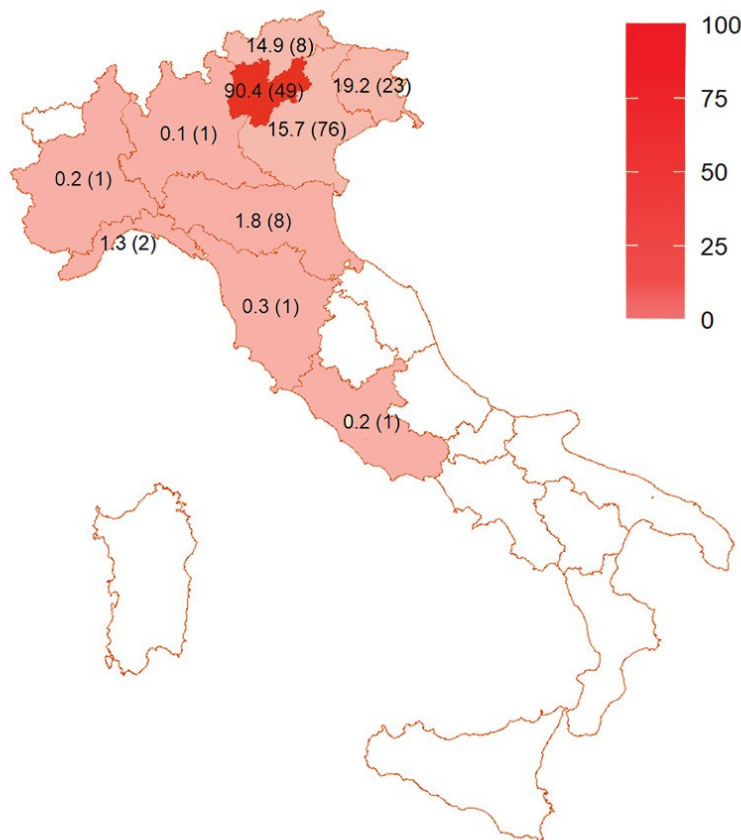
Table 1: TBE in Italy	
Viral subtypes, distribution	European TBEV subtype ¹⁹
Reservoir animals	Rodents, ticks
Percentage infected ticks	0.17% (Trento Province, ¹⁹); 2.1% (Belluno province, ²⁵).
Dairy product transmission	N/A
Case definition used by authorities	Case definition: Clinical criteria are any symptoms of inflammation of the CNS (for example, meningitis, meningo-encephalitis, encephalomyelitis, encephaloradiculitis). A TBE case is confirmed by at least one of the following five laboratory criteria: TBE specific IgM AND IgG antibodies in blood; TBE specific IgM antibodies in CSF; seroconversion or four-fold increase of TBE-specific antibodies in paired serum samples; detection of TBE viral nucleic acid in a clinical specimen; isolation of TBE virus from clinical specimen.
Type of reporting	Reported by Department of Infectious Diseases, National Institute of Health, Italy in collaboration with all the Infectious Diseases Units and Public Health Districts. Surveillance has been enhanced at the national level since 2017 and web-based from 2020. Presumed place of exposure and date of tick bite are recorded.
Other TBE surveillance	Ticks, rodents and sentinel animals screening.
Special clinical features	Bi-phasic disease is not reported.
Licensed vaccines	TICOVAC 0.5 mL and 0.25 mL (for pediatric use) (Pfizer Srl).
Vaccine recommendations	Vaccine is free of charge for residents in the Friuli-Venezia Giulia and Trentino-Alto Adige regions.
Vaccine uptake	Recommended for those who live, frequent or work in the woods or in rural areas i.e. hikers/trekkers, foragers, agricultural, forest or lumber workers.
National Reference center for TBE	Prof.ssa Anna Teresa Palamara Dipartimento Malattie Infettive Istituto Superiore di Sanità Viale Regina Elena, 299 00161 Roma, Italia https://www.iss.it

Figure 2: Age and gender distribution of reported human cases of neuro-invasive laboratory confirmed TBEV infections, Italy, 2020-2023.



Source Data: Appendix—Figure 2

Figure 3: Distribution (4-year incidence/100,000 and number of cases in 4 years (2020-2023)) of neuro-invasive laboratory confirmed TBE per region/autonomous province (incidence based on each region / province population size) of Italy



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Appendix

Source data: Figure 1

Year	Number of cases	Incidence/ 10 ⁵	Vaccination rate (%)
2000	12	0.021	
2001	24	0.042	
2002	9	0.016	
2003	17	0.029	
2004	32	0.055	
2005	25	0.043	
2006	44	0.074	0.11
2007	21	0.035	0.11
2008	26	0.043	0.11
2009	34	0.056	0.14
2010	21	0.035	0.13
2011	26	0.044	0.16
2012	34	0.057	0.10
2013	42	0.069	0.18
2014	22	0.036	0.15
2015	14	0.023	
2016	53	0.087	
2017*	24	0.04	
2018*	39	0.065	
2019*	24	0.040	
2020*	21	0.047	
2021*	18	0.032	
2022*	73	0.122	
2023*	49	0.083	

Source data: Figure 2

Age group (years)	Males	Females	All
0-9	2	0	2
10-19	8	6	14
20-29	4	5	9
30-39	11	1	12
40-49	13	5	18
50-59	26	18	44
60-69	26	10	36
>70	24	11	35

* Neuroinvasive laboratory confirmed TBEV infections

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