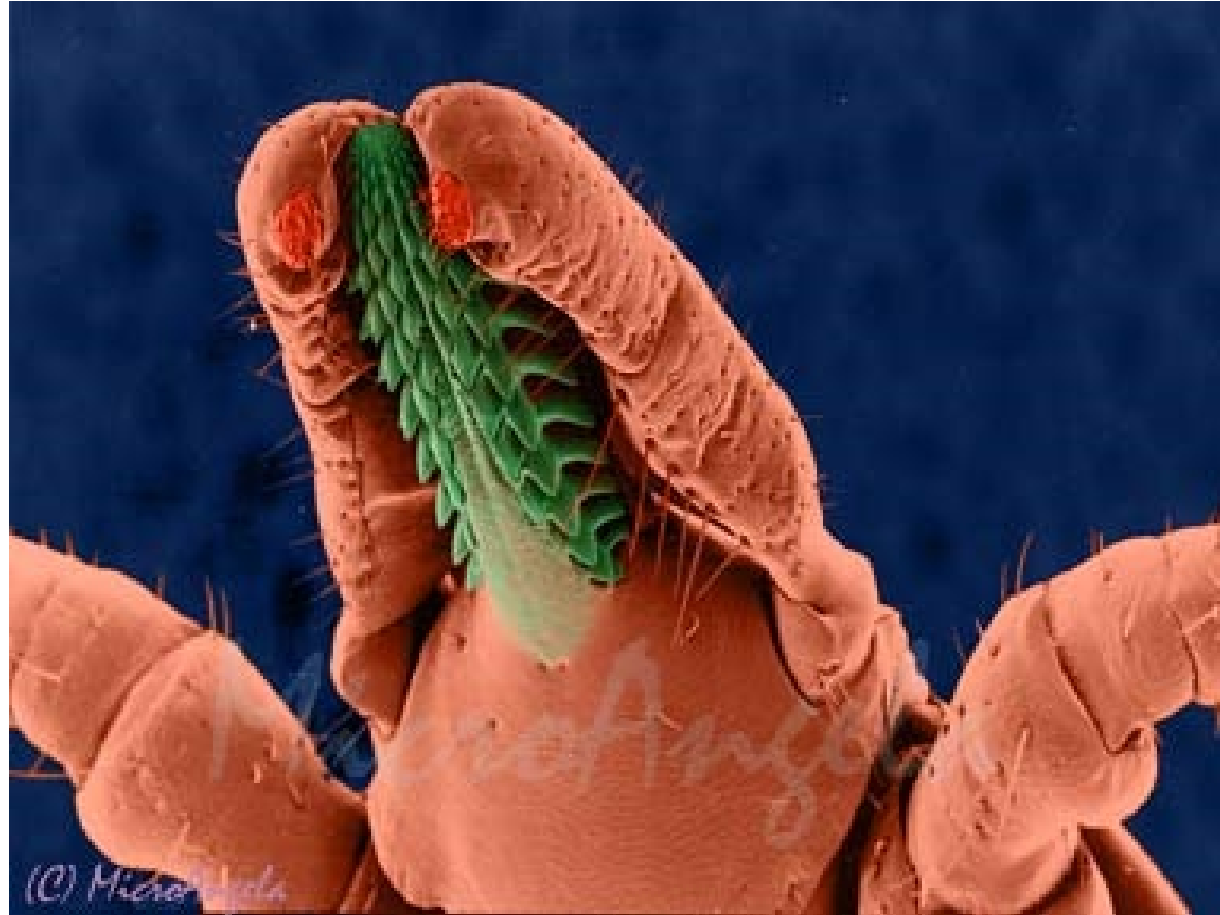


# Tick-borne encephalitis (TBE)

LL  
2022

## Clinical aspects

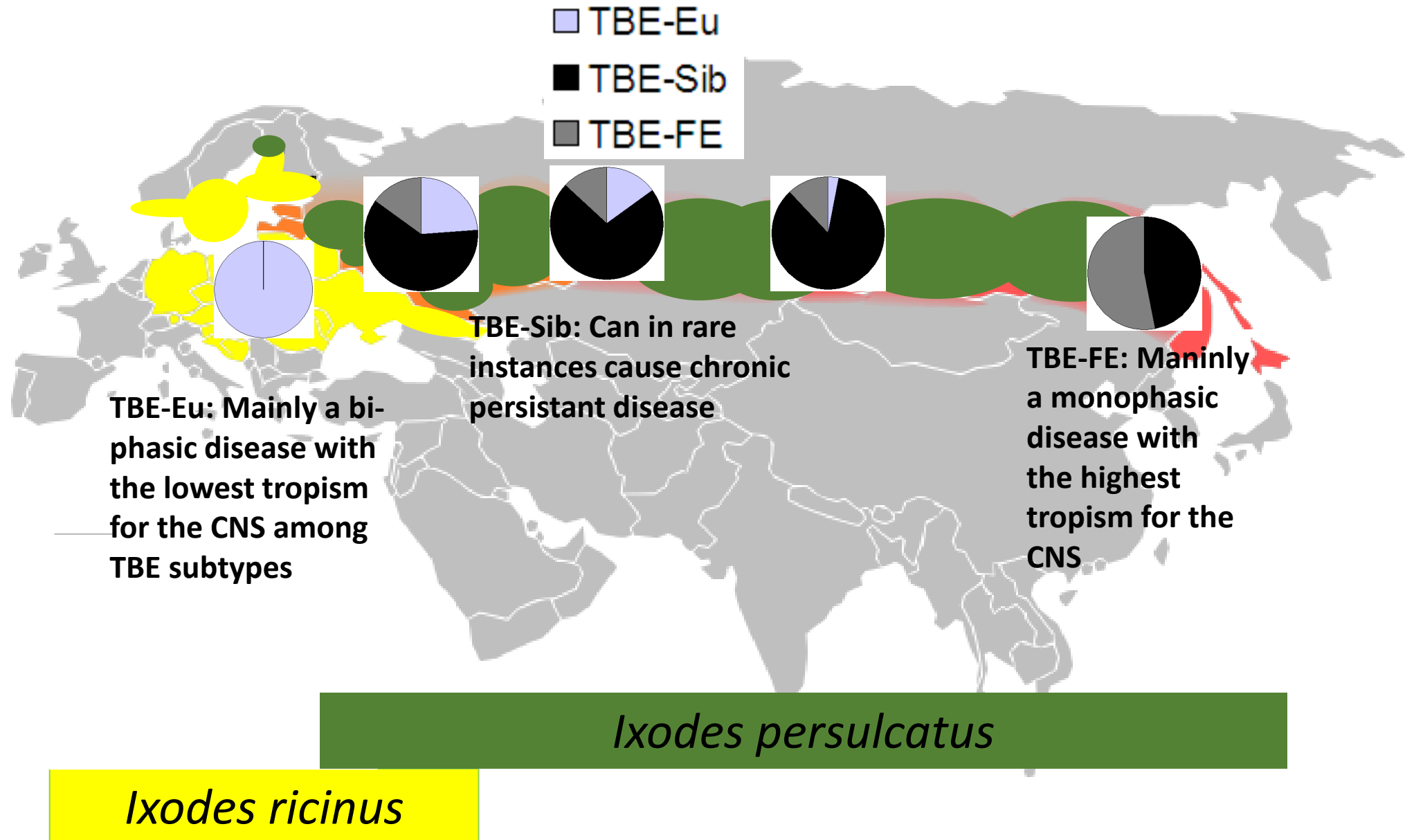


Webinar Lecture Sept 28, 2022, Lars Lindquist

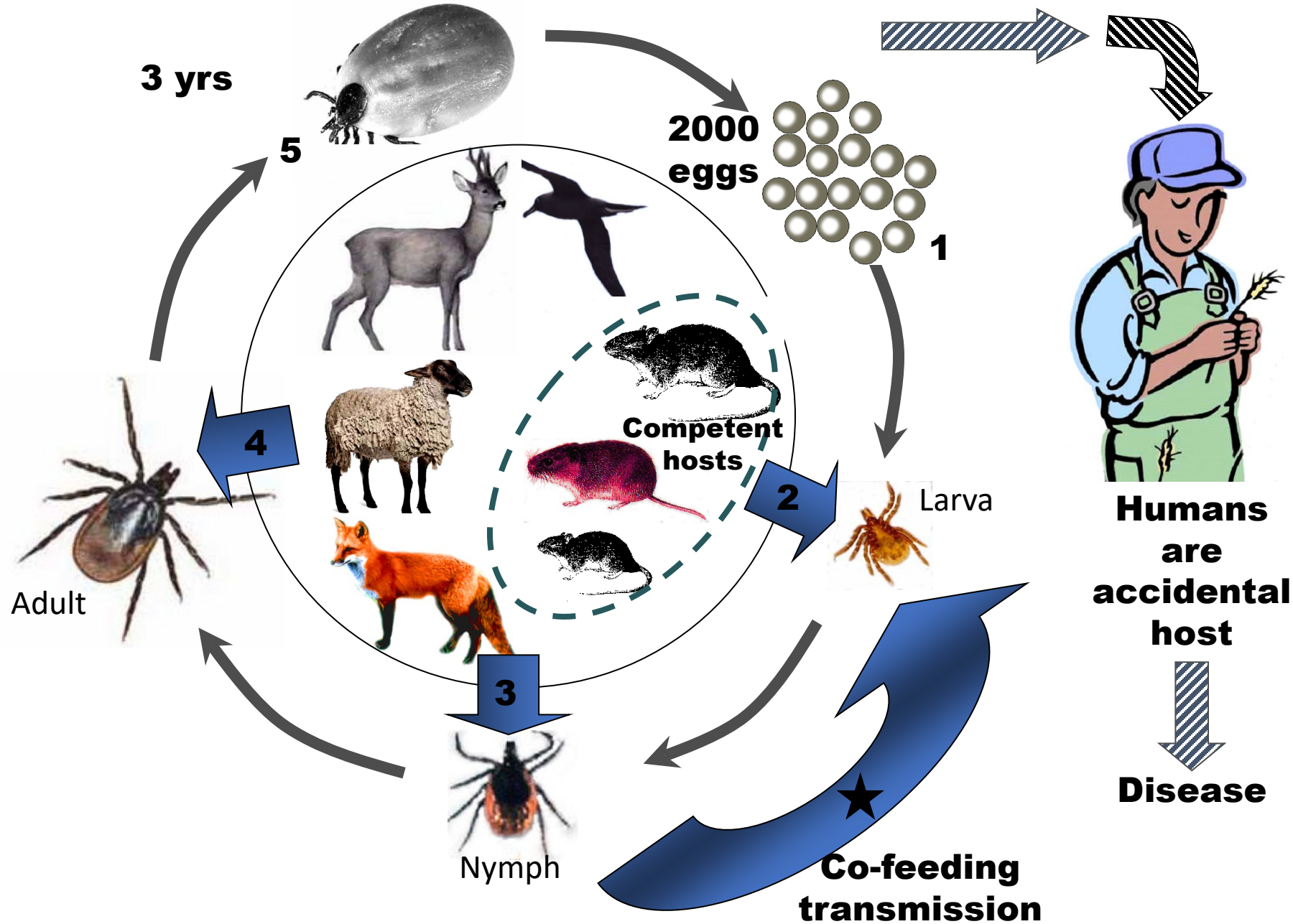
# Different subtypes of TBE and geographic distribution

## My talk will focus on TBE-Eu

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# The natural life cycle of the TBE virus



Man is not at all important for maintaining TBE virus in nature

# Case definition of TBE in humans

## CLINICAL CRITERIA

- Inflammation of the Central Nervous System (CNS) (including meningitis, encephalitis, myelitis or radiculitis)

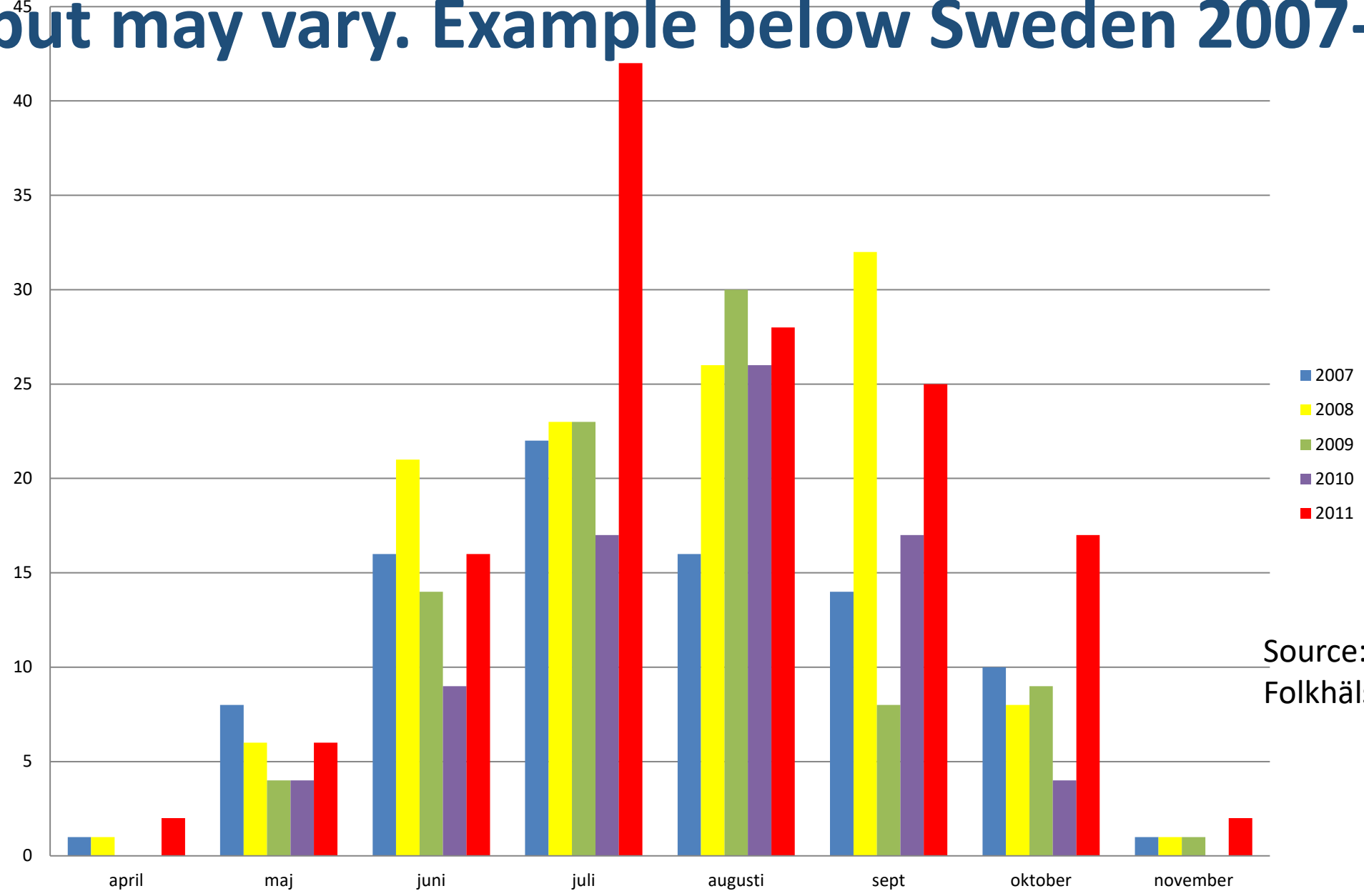
## LABORATORY CRITERIA

- Probable case:
  - Detection of serum TBE-specific IgM-antibodies. 96% are positive in the first serum sample.
- Confirmed case:
  - 4-fold increase of serum antibody levels (IgG )
  - Detection of specific intrathecal (spinal fluid) antibodies

**If suspicion of vaccine breakthrough** indication of testing intrathecal antibodies. If a vaccine breakthrough has occurred there is a risk of initial negative serum IgM-response and a boosted serum IgG-antibody response (second test taken after approx 10-14 days) is needed to confirm a TBE diagnosis To speed up the diagnosis therefore intrathecal antibody is therefore a possible alternative.

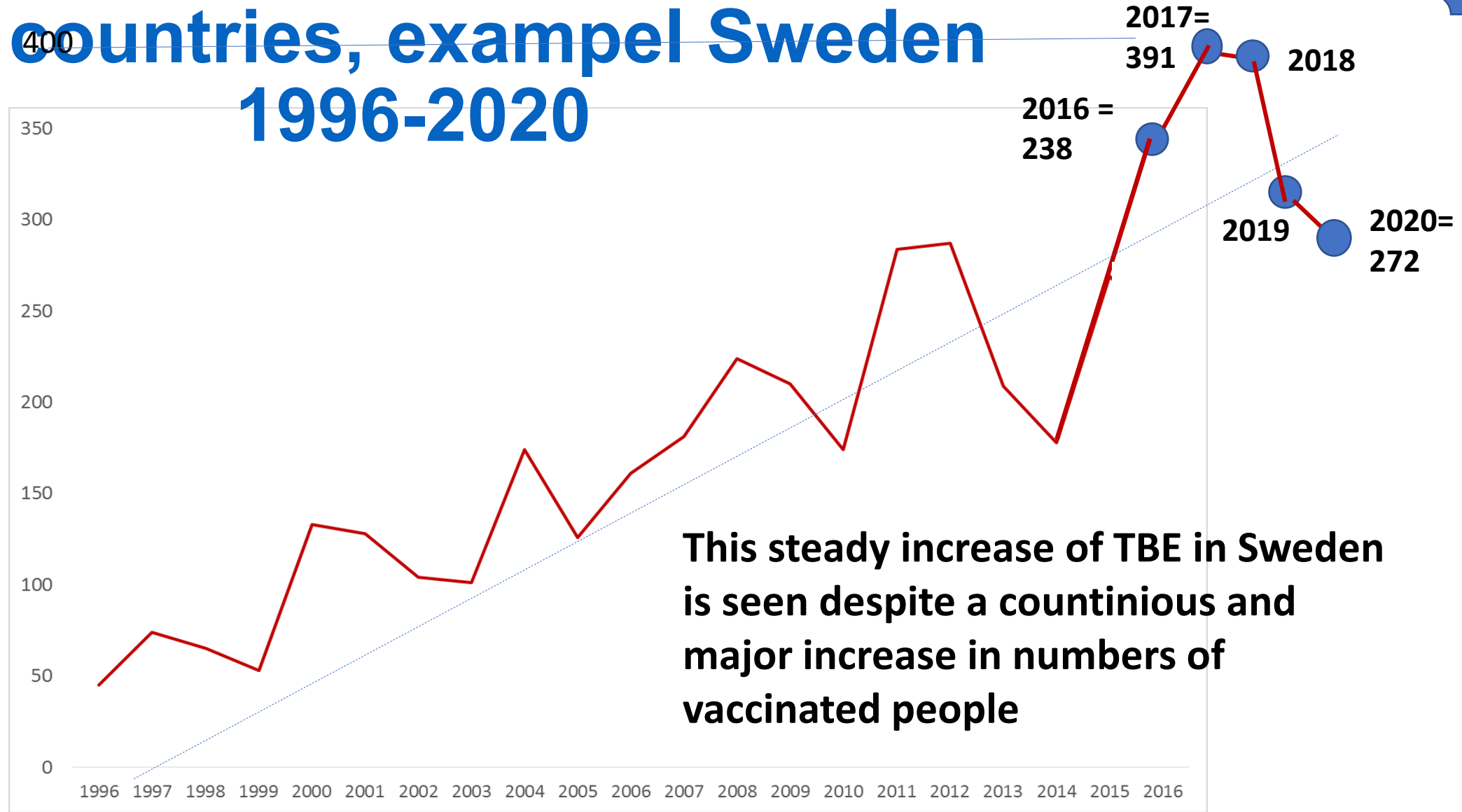
# TBE season in EU is April-November, peak month usually July but may vary. Example below Sweden 2007-2011

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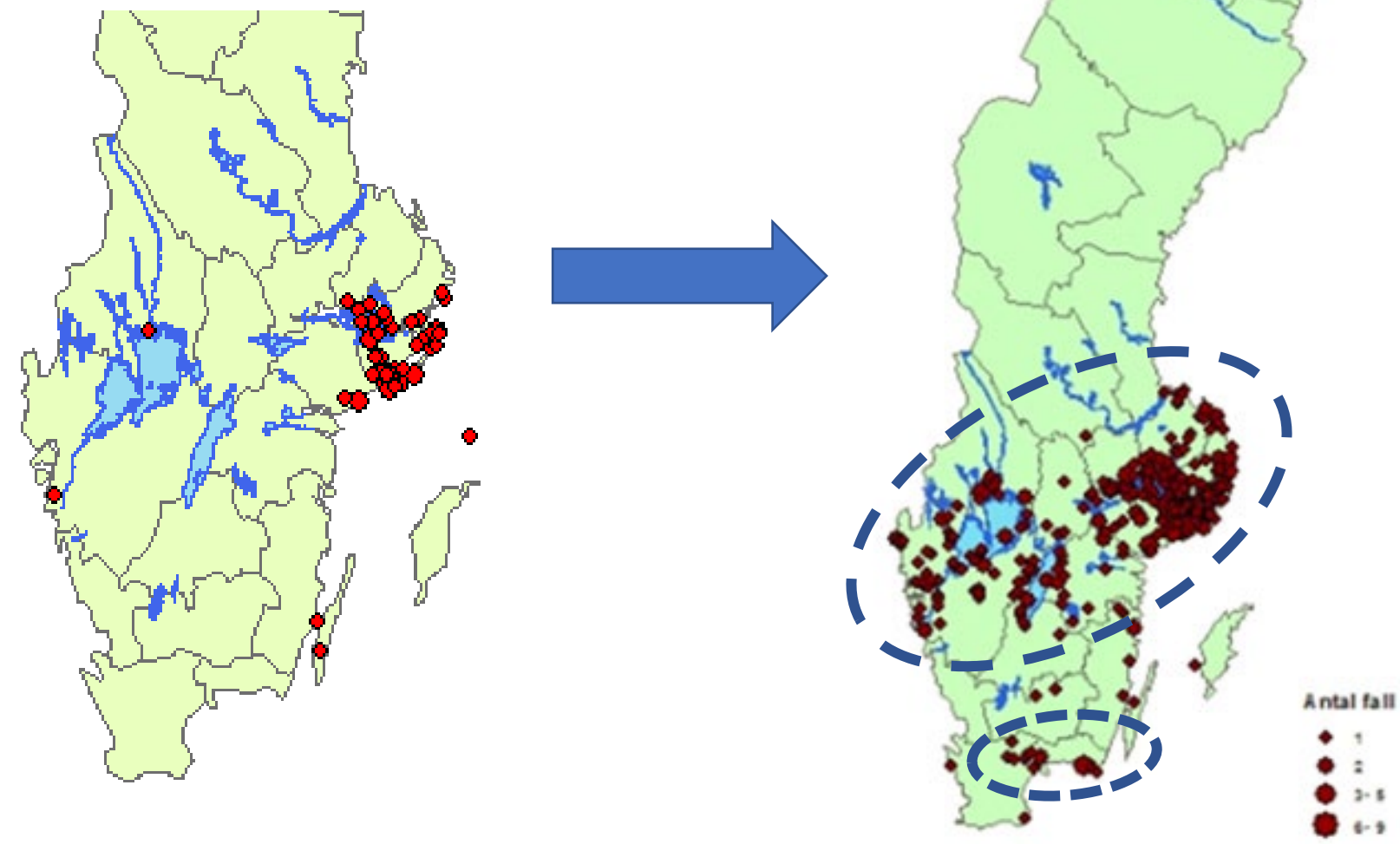
Source:  
Folkhälsomyndigheten

# An increased risk of TBE is seen in many countries, example Sweden 1996-2020



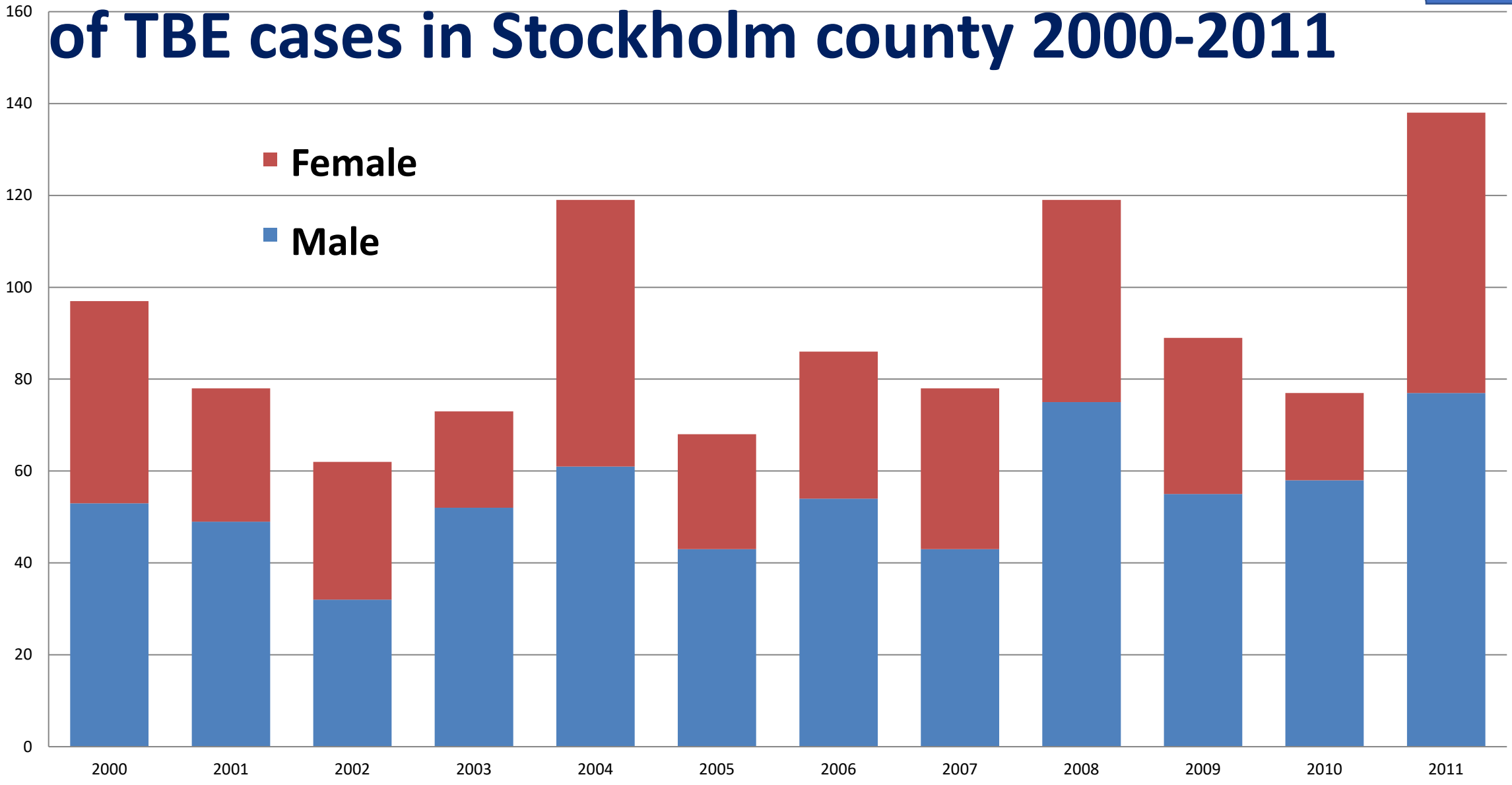
**This steady increase of TBE in Sweden is seen despite a continuous and major increase in numbers of vaccinated people**

There has also been a common regional spread of TBE over time. Below the situation in Sweden  
**1990** **2017**



Source:  
Folkhälsomyndigheten

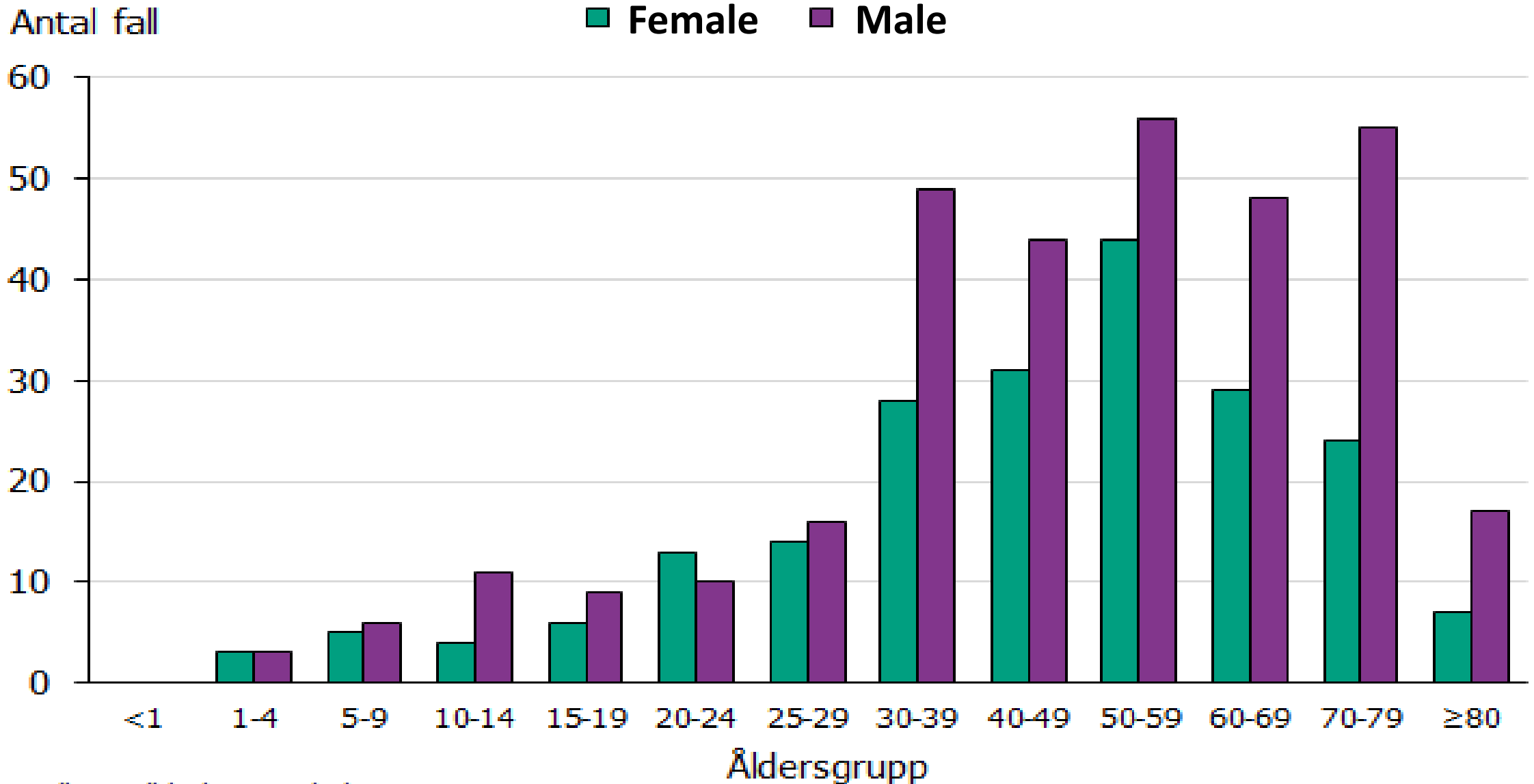
# The proportion of male (blue) and female (red) of TBE cases in Stockholm county 2000-2011





# Reported TBE cases are significantly higher in adults, especially in male cases (Sweden 2021)

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Källa: Folkhälsomyndigheten

# Different disease patterns of TBE

**Fever/ an influenza  
like illness**



**Only meningitis**



**Encephalitis**



**Myelitis**



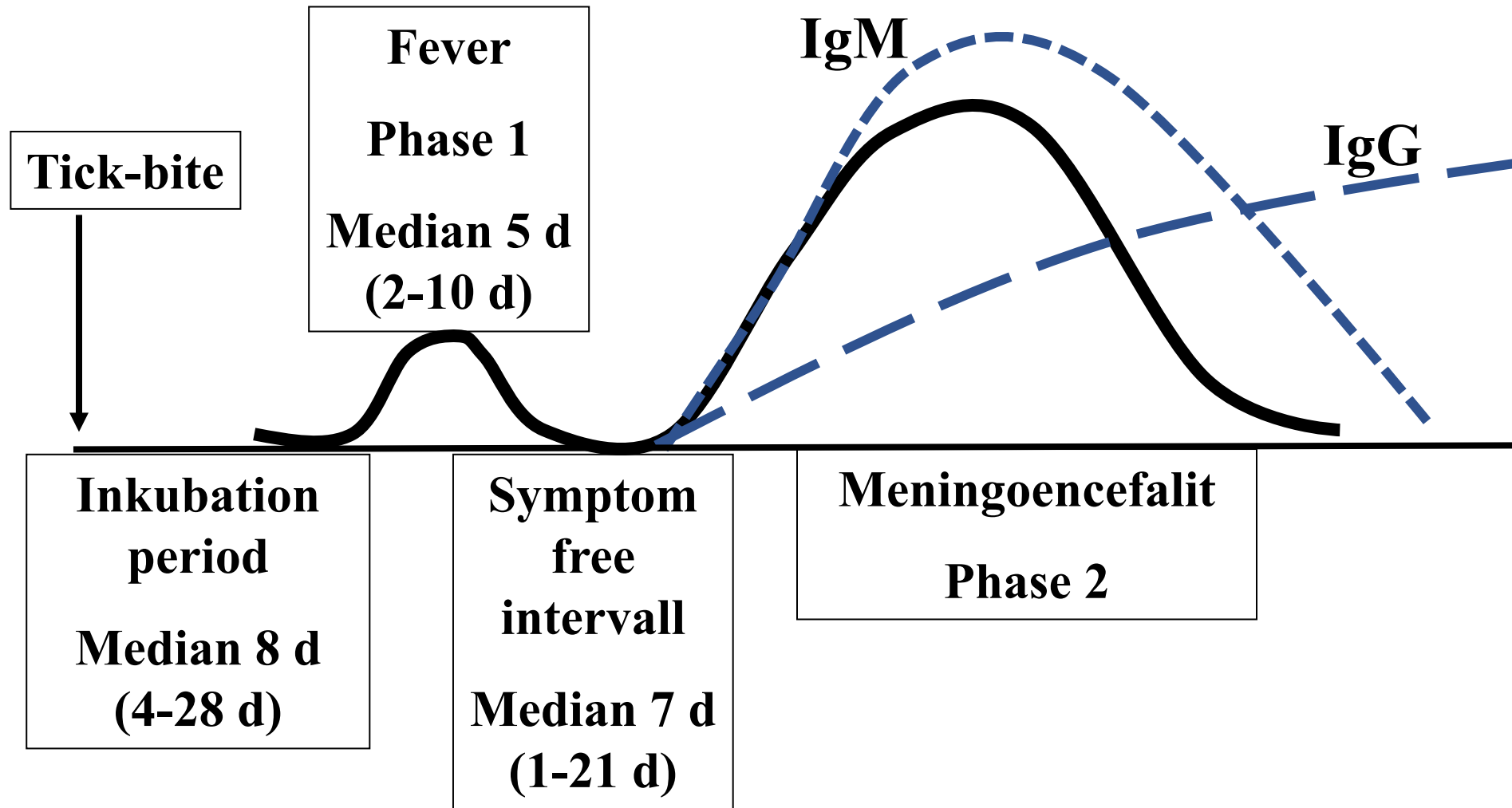
**Less severe forms of TBE**

**Severe forms of TBE**

# The overall clinical course in meningoencephalitis caused by the European Subtype of TBE (TBE-Eu)

- **Prodromal phase:** An acute disease with usually a biphasic course in TBE-Eu with a prodromal **febrile phase** with 5-7 symptomless days before the second clinical phase. The Siberian and Far Eastern subtypes are more likely to have no prodromal phase and have a monophasic course.
- **Clinical infection phase: Meningitis encephalitis, cerebellitis, or myelitis.** Most patients recover but some have residual symptoms, the most common is a cognitive post-infectious symptoms. The Siberian subtype of TBE is associated with a higher risk of chronic neurologic symptoms.

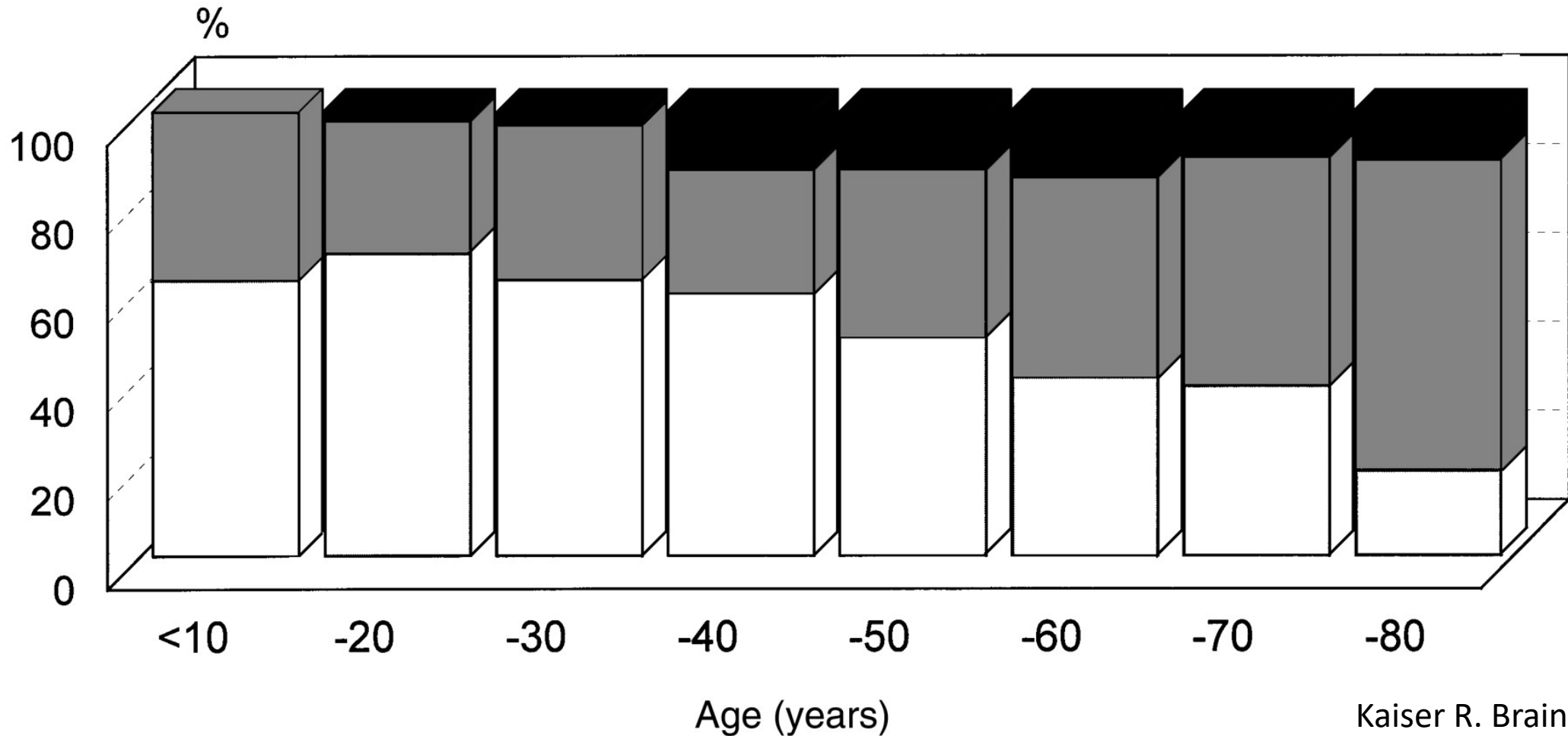
# The usual clinical course of TBE-Eu



This typical bi-phasic pattern is seen in 72-87%

# The proportion of more severe clinical symptomatology of TBE increase with age (study from southern Germany year 1994-98 (n=656))

□ Meningitis    ■ Meningoencephalitis    ■ Encephalomyelitis



# Fatal cases of TBE-Eu is unusual

- In a European study (*Euro Surveill. 2018 Nov 8; 23(45)*) of 11 623 confirmed cases of TBE 2012-2016 (of which 95% were hospitalized) a **case-fatality rate of 0,5%** was seen and **2,5% had neurological sequelae**.
  - None of the 20 fatal cases with know vaccination status were vaccinated except one that had recieved only one TBE-vaccine dose
- Of 2941 Swedish cases (*Vernaité R et al Emerg Infect Dis 28(7), 2022*) a **mean death rate** (year 2004-2017) of **0,75%** was seen with an increasing fatality rate by age. **The fatality rate 80-89 yrs of age was 3,45%. No fatal cases <40 yrs of age was seen in this summary.**

# Follow-up studies of adult patients with TBE in Sweden and Lithuania

- 1/3 have consisting symptoms of variable degree at follow up after 1-5 years
- Approximately 10% have signs of major neurological damage
- 1-2% are fatal
- 2-6% have a consisting paralysis

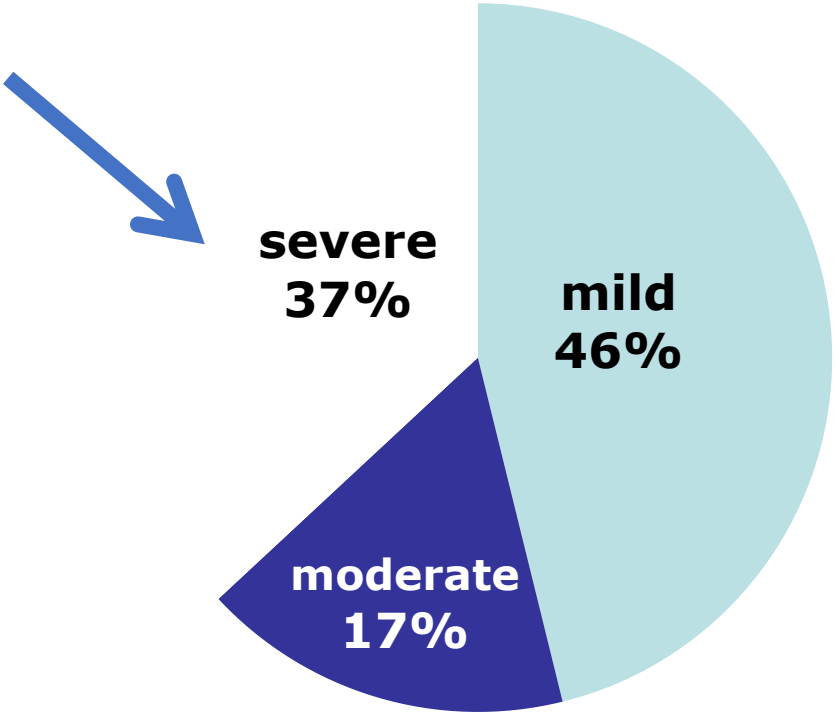


# Risk factors for severe TBE with long lasting or permanent sequelae

- Severe disease on admission
- Age >50 years
- Slow development of neutralizing antibodies
- Monophasic disease



# Study of 66 Swedish children with TBE – the proportion of children with mild, moderate or severe symptoms on admission



**Mild** = meningit

**Moderate** = meningitis symptoms with siezures or focal neurology or a pathological EEG

**Severe** = encefalitis

Åsa Fawler, The journal of Pediatrics, Jan 17 2013

**Number/percentage of TBE are a fairly low in children,  
and even more so below 7 years of age.**

**Below, confirmed TBE cases in Stockholm county in  
different age groups 2006 - 2011**

<b>Age</b>	<b>2006</b>	<b>2007</b>	<b>2008</b>	<b>2009</b>	<b>2010</b>	<b>2011</b>	
<b>&lt; 7 yrs</b>	2 (3%)	2 (3%)	2 (2%)	6 (7%)	4 (5%)	<b>5 (3,6%)</b>	} <b>13,7%</b>
<b>7-11 yrs</b>	5	7	11	4	3	<b>8 (5,8%)</b>	
<b>12-18 yrs</b>	9	6	5	5	3	<b>6 (4,3%)</b>	
<b>&gt;18 yrs</b>	70	60	101	74	68	119 (86,2%)	
<b>Totalt</b>	86	78	119	89	78	138	

# Fatal cases in children are uncommon

I have found only 2 fatal cases in children reported up to 2010

- 11-year old child with brain stem encephalitis in connection with surgery due to suspected appendicitis (*Messner et al. 1981*)
- 12-year old boy under treatment with corticosteroides due to histiocytosis (*anectotal report*)

# Summary of 12 consecutive (prospective\* or retrospective) studies of TBE in children up to 15 years of age

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Author/Country	Year of study	Severe disease	Age of severe disease	Sequelae
Harasek/Austria	1963-1973	2/38 (5,3%)	11 + 12 yrs	1
Falk/Austria	1975-1979	5/80 (6,3%)	7-15 yrs	0
Helwig/Germany	1971-1983	3/13 (24%)	7-15 yrs	0
Messner/Austria	1974-1979	2/93 (2,2%)	2 of which 1 <7 yrs	1 fatal (11 år)
Rakar/Slovenia	1978-1992	15/146 (10,3%)	7-15 yrs	6 (all ≥7 years)
Cizman/Slovenia	1993-1998	7/133 (5,2%)	7 of which 1 <7 yrs	4 (all ≥7 years)
Kaiser/Germany*	1994-1998	14/77 (18,2%)	?	?
Kaiser/Germany*	1994-2003	?/124		8 of which 1 severe
Tomazic/Slovenia*	1994	1/77 (1,3%)	?	?
Lesnicar/Slovenia	1959-2000	14-25/371 (3,8 – 6,7%)	?	0
Fritsch/Austria	1981-2005	11/116 (9,5%)	?	2 of which 1 severe (5 yrs)
Stähelin-Massik/Switzerland	2000-2004	2/55 (3,6%)	6 weeks + 9 yrs	1 (9 yrs)
<b>TOTAL</b>		<b>Mean 8,0%</b>	<b>Of 8% ≤15 yrs with severe disease only 1/10 was &lt;7 yrs</b>	<b>23/1246 (1,8%) of which 1 child &lt;7 år</b>

# Even though children with TBE-Eu usually have a mild acute disease follow-up of TBE cases in children (at Karolinska Hospital, Sweden) show risk of remaining problems

- **Remaining problems were seen in approx. 70% of children (n=42) 3-17 years old (mean 10 years old) at follow-up after 2-6 years.**
  - Headache approx. 60%
  - Cognitive problems approx. 60%
    - Memory
    - Concentration
  - 33% had problems with executive functions
  - Tiredness 45%
  - Irritability 42%
- **Also those children with a relative mild acute disease could show remaining problems at follow-up** (Fowler et al, J Pediatr, 2013)

## Conclusion of study in children with TBE at Karolinska Hospital Stockholm, Sweden was:

- Children often had a vague symptomatology (bad feeling in general, headache, fever, tiredness). Children also had more difficulties to explain their problems.
- TBE is probably an under diagnosed disease in children.
- Long-term symptoms, mostly cognitive disorder, was seen also in children, and the number of children with cognitive sequelae was surprisingly high.

Sundin et al, 2011

Hansson et al, 2011

A scenic view of a rocky coastline with blue water and a clear blue sky. The text "Thank you!" is overlaid in the center.

**Thank you!**