WEST NILE DISEASE: SORVEGLIANZA INTEGRATA IN REGIONE LOMBARDIA

12 dicembre 2014- Izsler Brescia

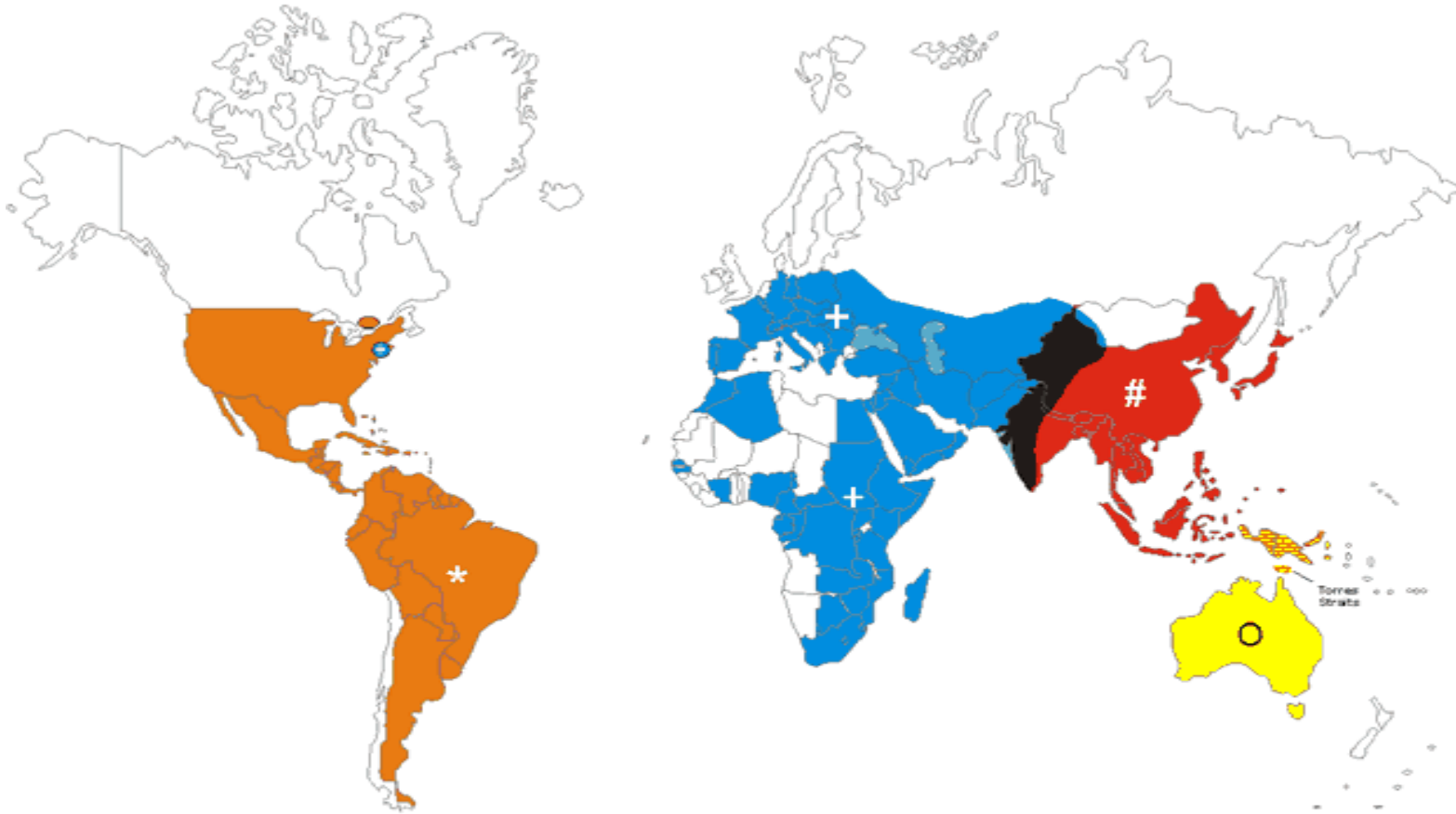
Epidemiologia delle infezioni da flavivirus negli ultimi dieci anni in Nord Italia.

Michele Dottori

Flavivirus trasmessi da zanzare

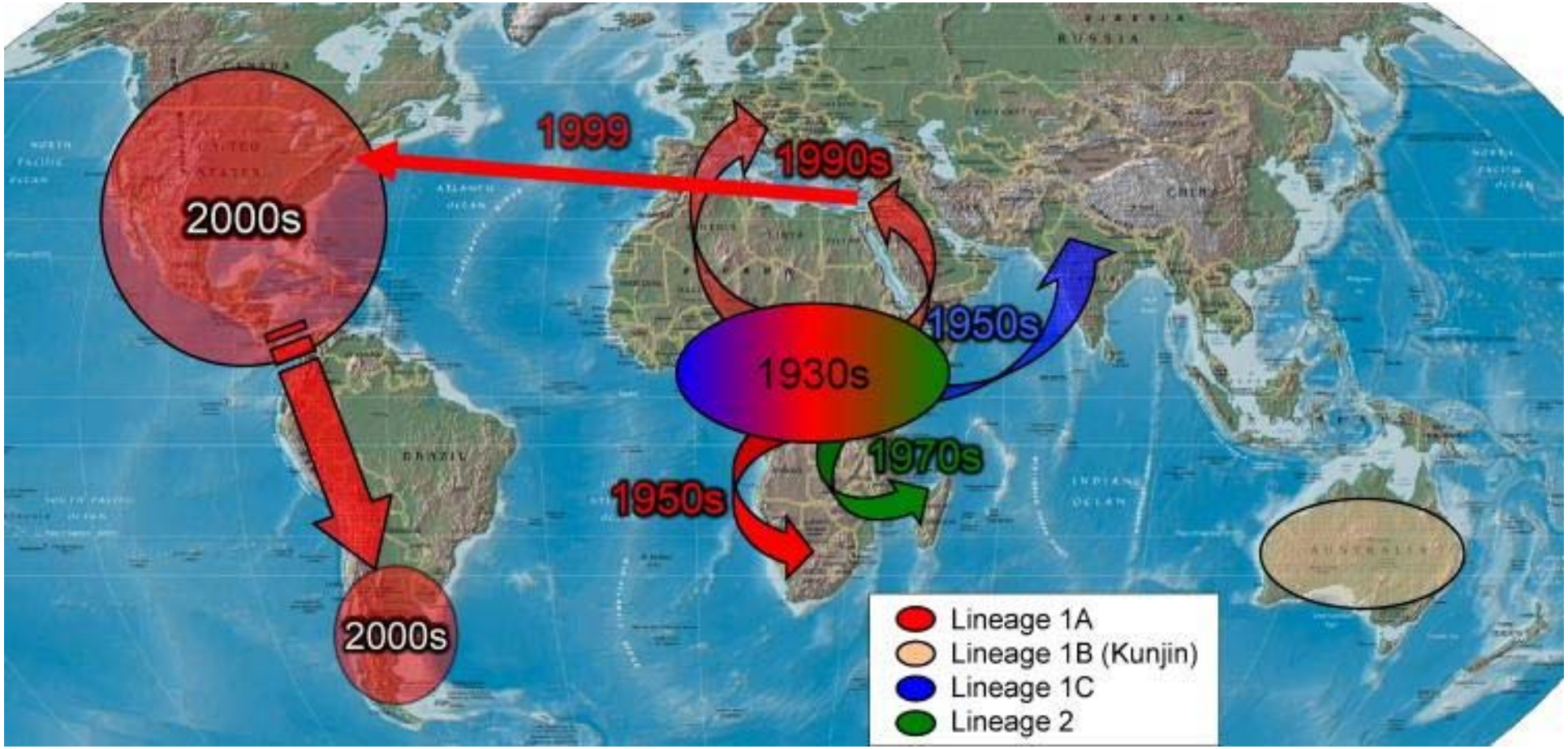
Virus	Principali specie vettrici	Serbatoi	Diffusione
Dengue	*Aedes aegypti* , *Ae. albopictus, Aedes* spp	Uomo	Africa, Americhe, Asia
Encefalite della Murray Valley	*Culex annulirostris*	Volatili	Australia, Nuova Guinea
Encefalite giapponese	*Culex tritaeniorhynchus* , *Culex* spp.	Volatili, maiali	Asia
Encefalite St. Louis	*Culex pipiens Culex nigripalpus Culex* spp.	Volatili	Americhe
Febbre gialla	*Aedes aegypti* , *Aedes africanus, Aedes* spp.	Primati	Africa, America centro-meridionale
Ilheus	*Psorophora ferox, Psorophora* spp *Ochlerotatus* spp	Volatili (selvatico)	Americhe
Kunjin	*Culex annulirostris*	Volatili	Australia, Nuova Guinea
Rocio virus	*Ochlerotatus scapularis* , *Psorophora fero* x	?	Brasile
Spondweni	*Mansonia africana, M uniformis altre specie*	?	Sud Africa
Usutu	*Culex* spp.	Volatili	Africa, Europa
Wesselsbron	*Aedes* spp.	Volatili, mammiferi	Africa del Sud
West Nile	*Culex* spp.	Volatili	Tutto il mondo
Zika	*Aedesafricanus, Ae luteocephalus, Ae aegipty, Aedes* spp	Primati	Africa Sud-Est Asiatico

The Geographic Distribution of the Japanese Encephalitis Serocomplex of the Family Flaviridae, 2000.



- St. Louis encephalitis
- * Rocio and St. Louis (Brazil)
- + West Nile virus
- # Japanese encephalitis
- West Nile and Japanese encephalitis
- Japanese and Murray Valley encephalitis
- O Murray Valley and Kunjin

WNV



Da Weaver and Reisen 2010

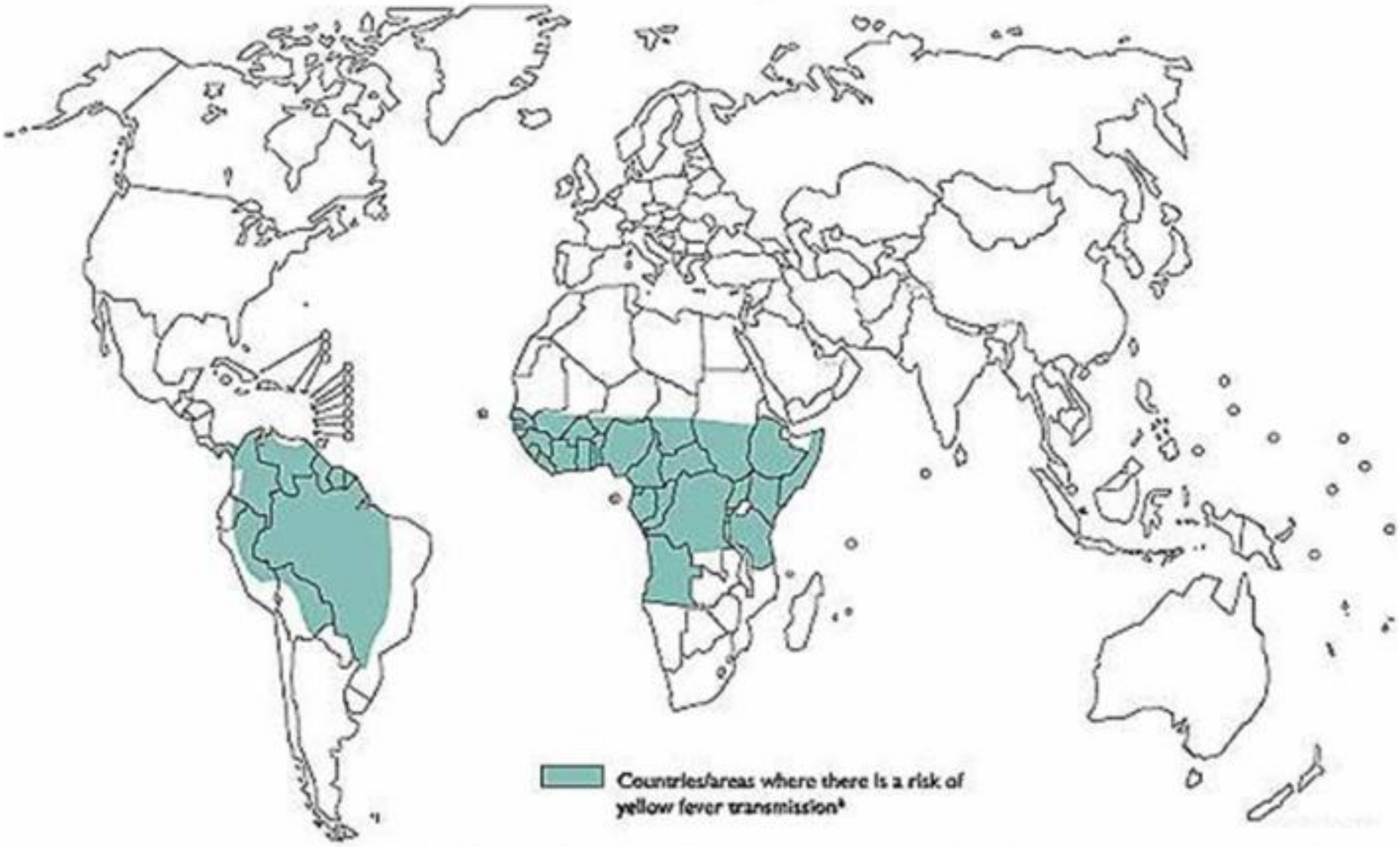
Japanese encephalitis, countries or areas at risk*

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization/CDC
Map Production: Public Health Information and Geographic Information Systems (GIS)
World Health Organization

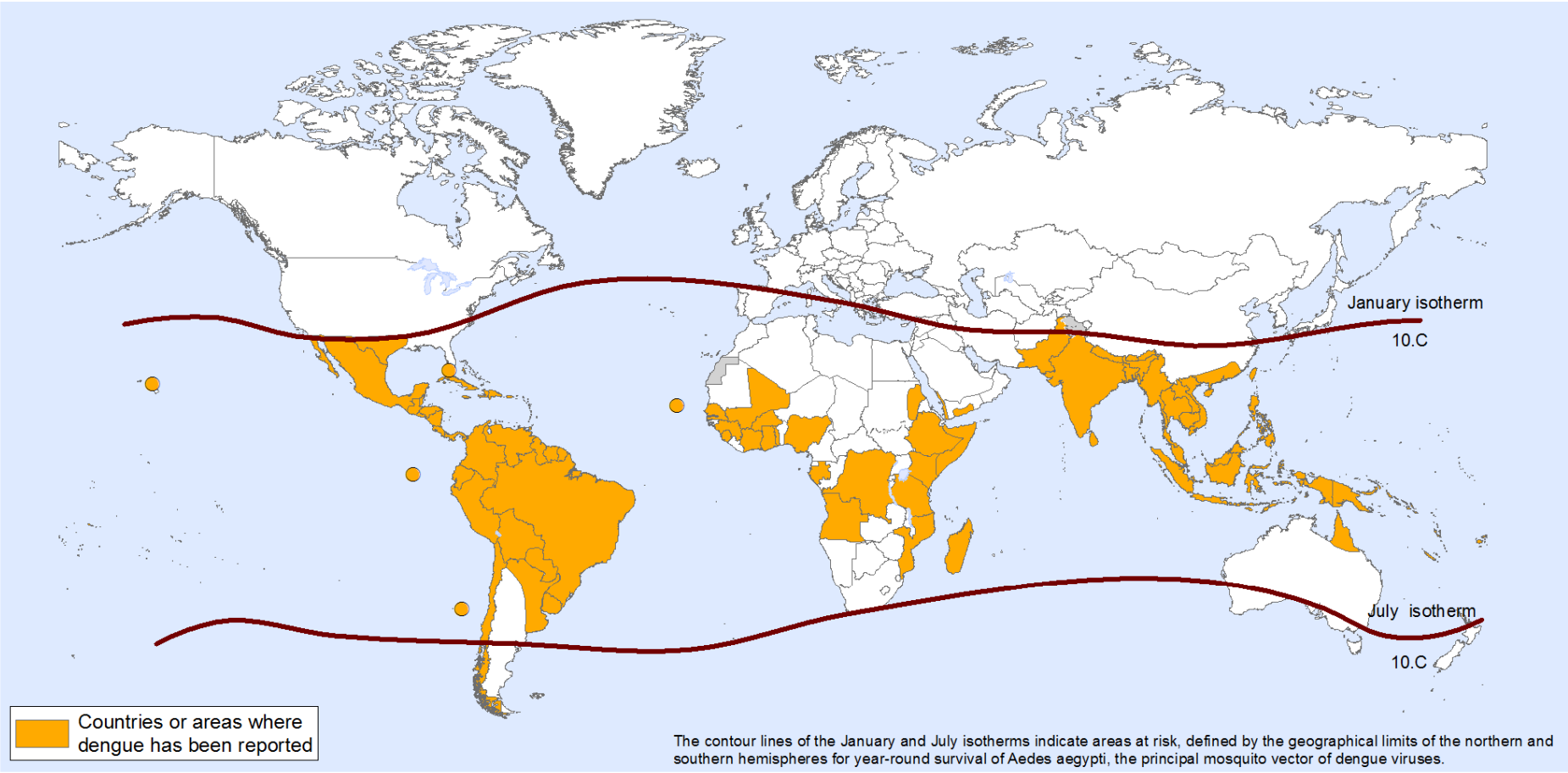
World Health Organization

Areas at risk of Yellow Fever transmission



[a] Either yellow fever has been reported or the presence of vectors and animal reservoirs creates a potential risk of infection (considered to be endemic areas).

Dengue, countries or areas at risk, 2013



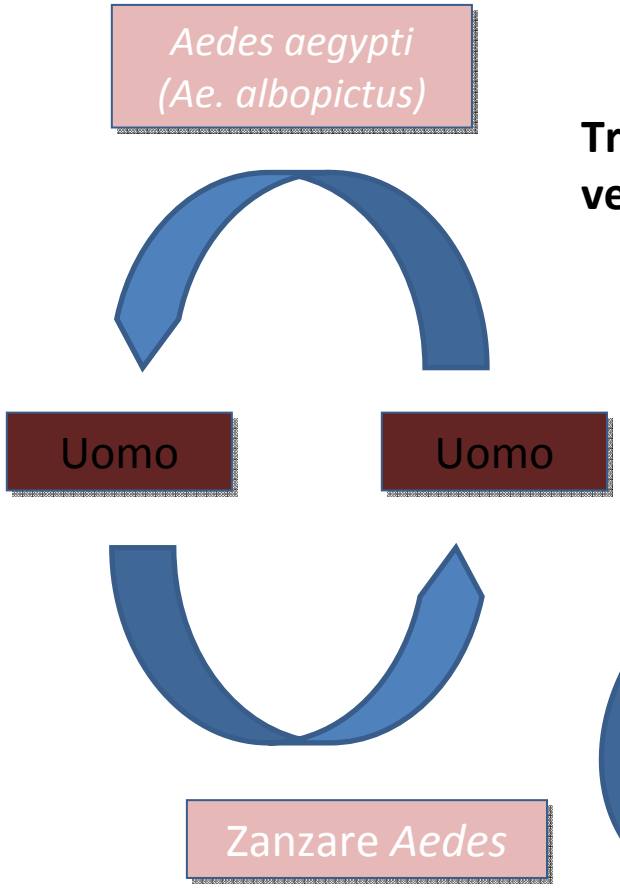
The contour lines of the January and July isotherms indicate areas at risk, defined by the geographical limits of the northern and southern hemispheres for year-round survival of Aedes aegypti, the principal mosquito vector of dengue viruses.

Data Source: World Health Organization
Map Production: Health Statistics and Information Systems (HSI)
World Health Organization

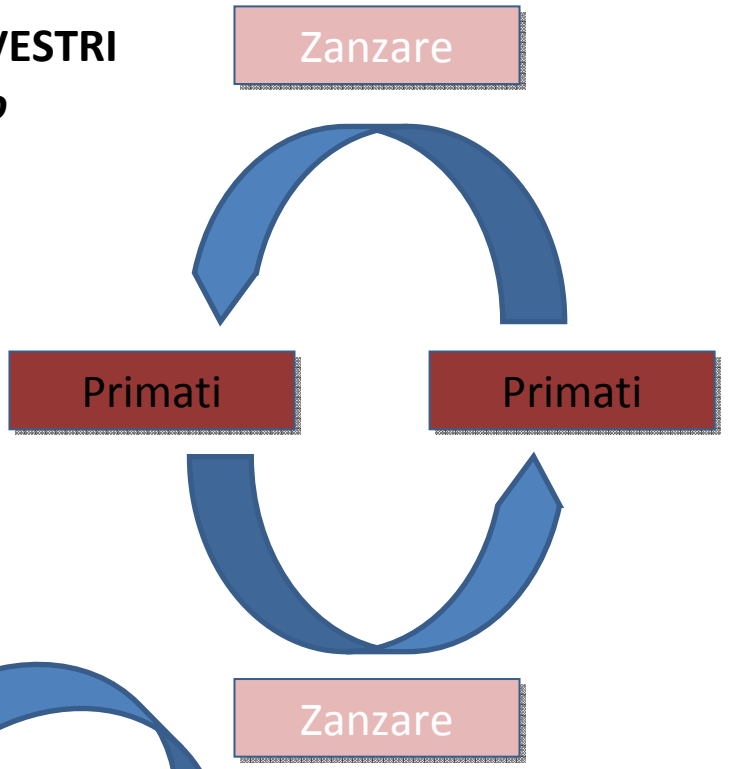
World Health Organization

CICLI - DEN

AMBIENTI URBANI
Epidemico/endemico

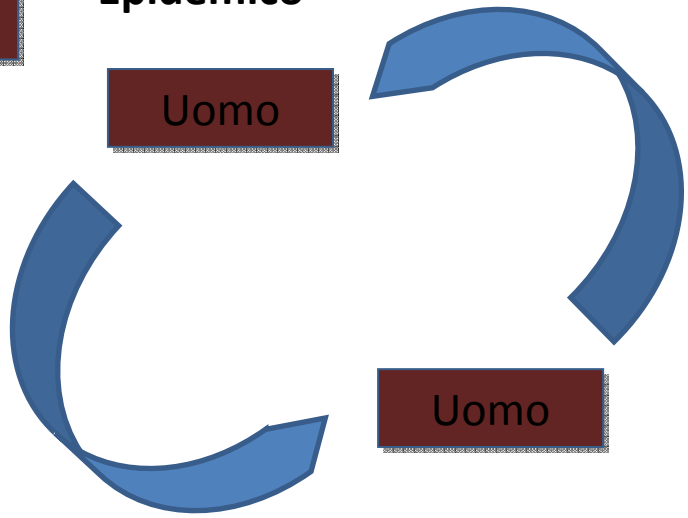


AMBIENTI SILVESTRI
Ciclo enzootico
(Asia-Africa)



Trasmissione
verticale nei vettori

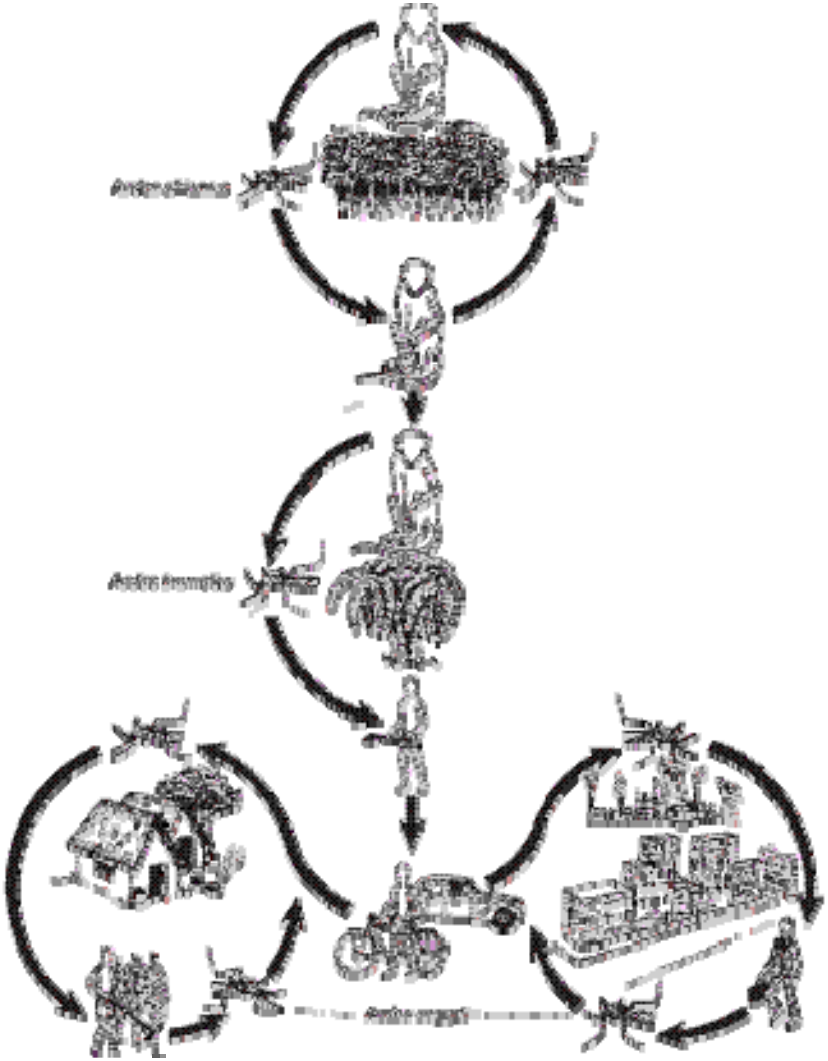
AMBIENTI RURALI
Epidemico



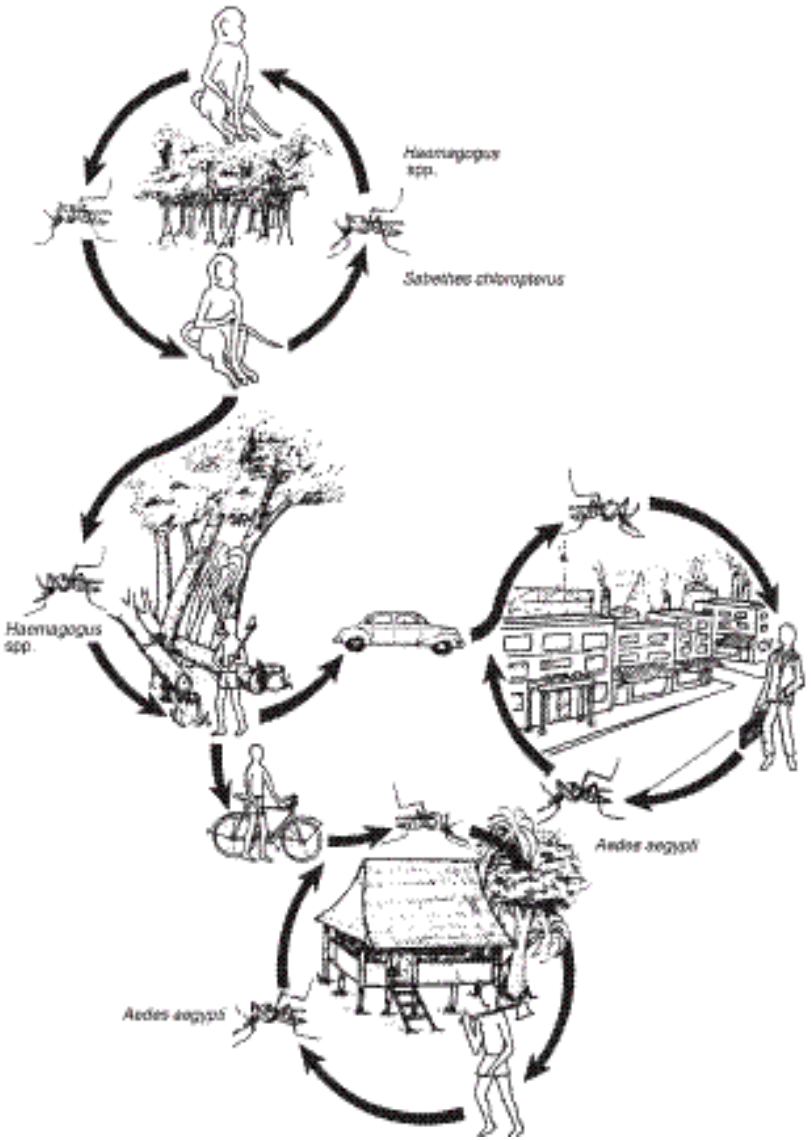
Modificato da V. Deubel e B. Murgue

Jungle, rural and urban transmission cycles of yellow fever

Africa



Central and South America



Fattori influenzanti

CRESCITA DEMOGRAFICA

(ANTROPIZZAZIONE, DEFORESTAZIONE)

GLOBALIZZAZIONE

(TURISMO, AFFARI, IMMIGRAZIONE, TRASPORTI)

CAMBIAMENTI CLIMATICI

(PIOVOSITÀ, TEMPERATURE, PROLUNGAMENTO DELLA STAGIONE FAVOREVOLE)

ATTIVITÀ OUTDOOR

Vie di importazione in Europa

1. Viaggiatori viremici
2. Commercio di vertebrati potenzialmente infetti (zoo, animali domestici, bestiame)
3. Introduzione di zanzare infette (larve, uova,adulti) con aereoplani navi, autoveicoli.
4. Uccelli migratori infetti (WNV)

Da Hubalek 2006

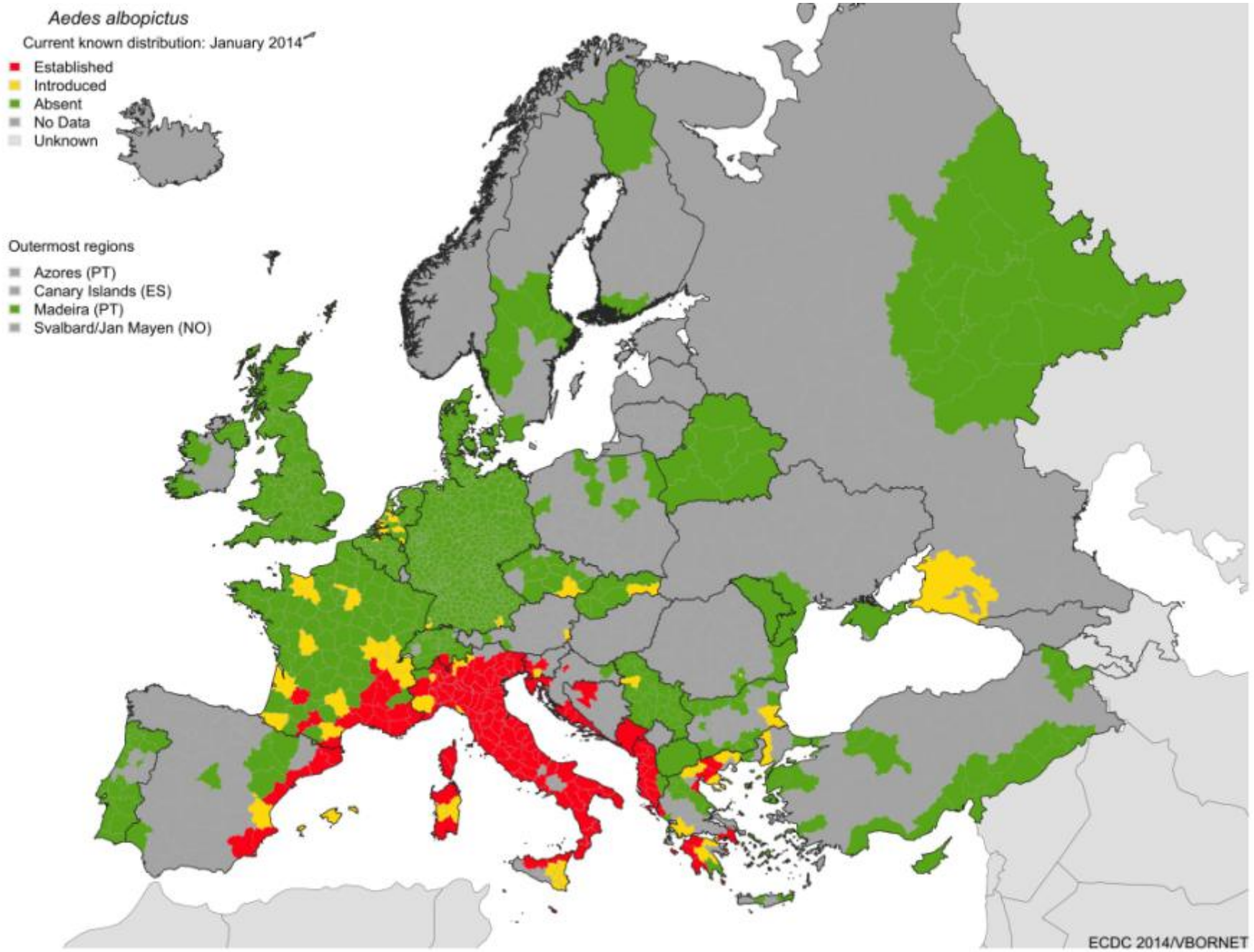

Aedes albopictus
Current known distribution: January 2014
Established
Introduced
Absent
No Data
Unknown
Outermost regions
Azores (PT)
Canary Islands (ES)
Madeira (PT)
Svalbard/Jan Mayen (NO)
ECDC 2014/VBORNET

Tabella 1. Casi importati di febbre Chikungunya e Dengue in Italia, nel 2011-2013

Regione	2011		2012		2013	
	Chikungunya	Dengue	Chikungunya	Dengue	Chikungunya	Dengue
Piemonte	0	1	0	5	0	12
Lombardia	1	3	0	25	2	42
P.A. Trento	0	0	0	0	0	1
Veneto	0	11	5	12	0	17
FriuliVenezia Giulia	0	4	0	0	0	0
Emilia-Ro magna	1	16	0	11	1	24
Toscana	0	5	0	10	0	15
Umbria*	0	0	0	1	0	0
Marche	0	0	0	1	0	0
Lazio*	0	4	0	14	0	25
Puglia	0	3	0	0	0	5
Sicilia	0	0	0	0	0	1
Totale	**2**	**47**	**5**	**79**	**3**	**142**

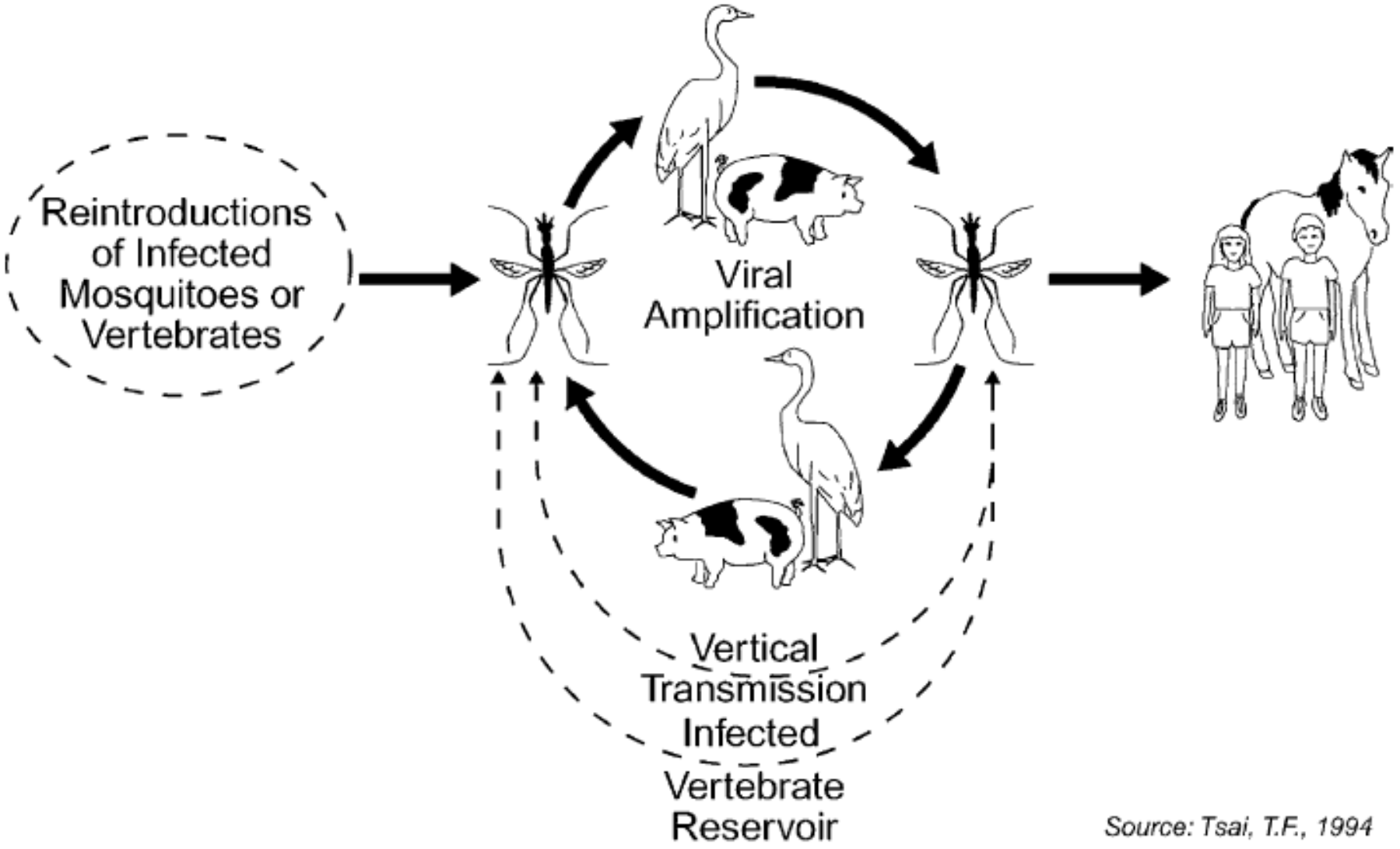
* Dati non confermati dalle regioni

Dati dalla circolare del Ministero della Salute “Sorveglianza dei casi umani delle malattie trasmesse da vettori con particolare riferimento alla Chikungunya, Dengue, Zika virus e West Nile Disease - Giugno 2014”

Zanzara tigre non è il principale vettore di DENV (trasmesso principalmete da *Aedes aegypti*)

Trattamenti adulticidi attorno ai casi umani importati

JE



Source: Tsai, T.F., 1994

Usutu virus

Since 2009, both systems recorded the circulation of Usutu virus (USUV), a flavivirus closely related to WNV with a not yet defined pathogenic capacity

Vectors: mosquitoes especially *Culex* (*Culex pipiens*)

Reservoirs: wild birds

Possible mass mortality in birds (blackbird)(Austria 2001).

WNV differential diagnosis (it can be cross-reactive also in PCR)

Human disease: 2 cases of encephalitis reported in immunosuppressed individuals in Italy in 2009 (Pecorari et al. 2009, Cavrini et al. 2009)

Anti-USUV response in healthy persons were recorded in ER, 4/359 in 2009; 14/6000 in 2010-11 (Gaibani et al. 2012, Pierro et al. 2013)

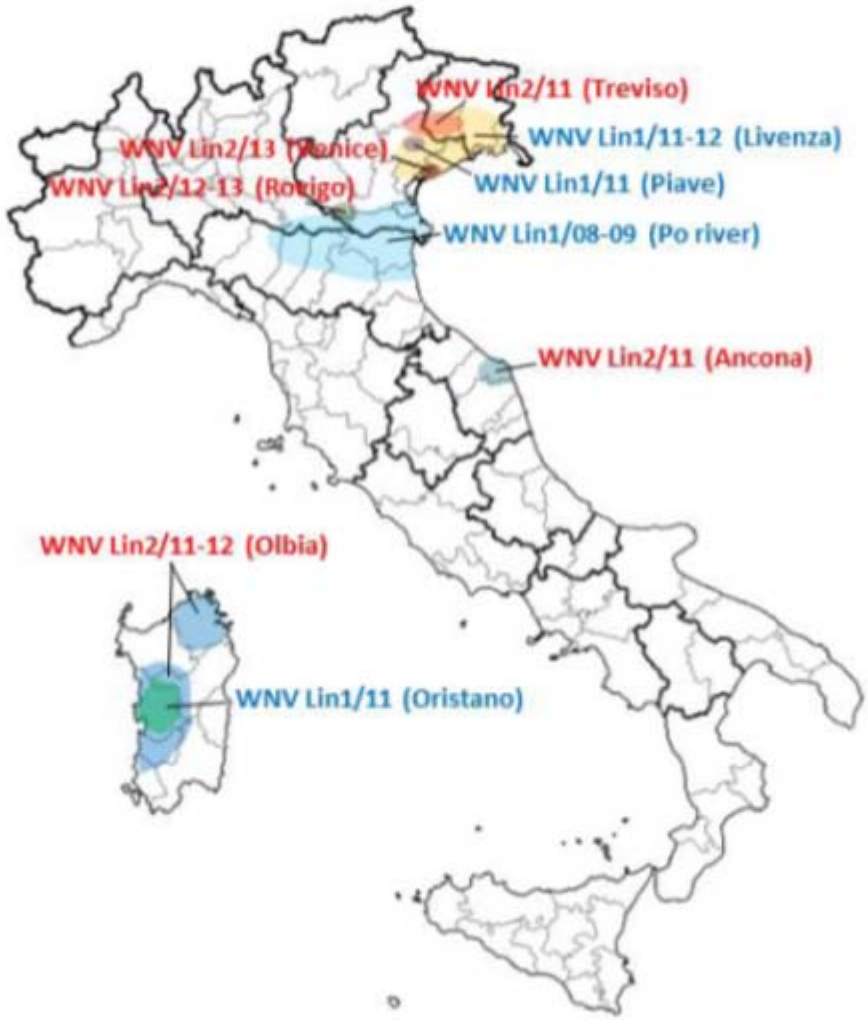
Isolates of West Nile virus from hematophagous arthropods (1999)

http://www.cdc.gov/ncidod/EID/vol5no5/hubalek.htm#Table%201

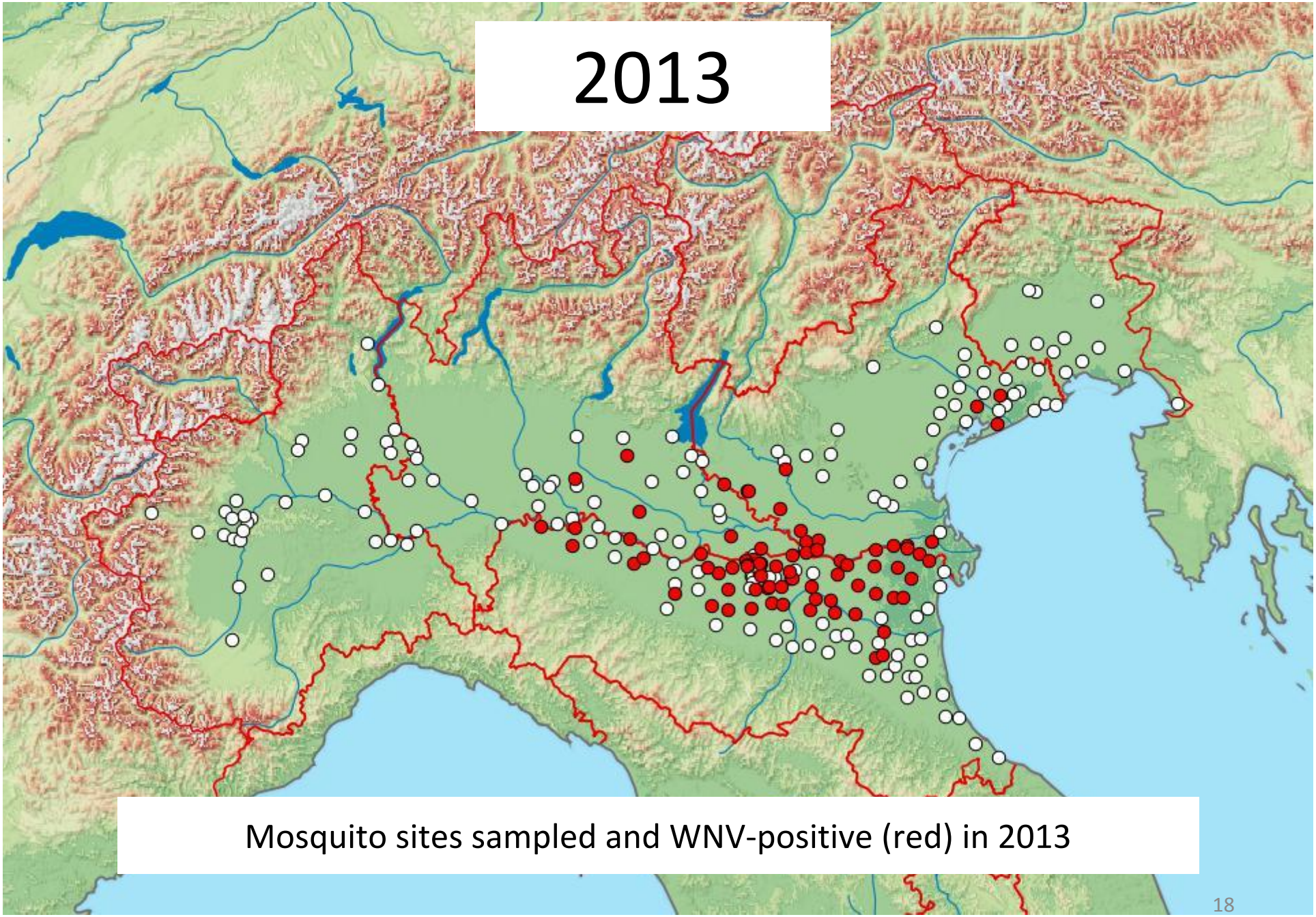
Mosquitoes species	N°	Paesi
Culex antennatus[a]	6	Egypt, Madagascar
decens group	8	Madagascar
ethiopicus	1	Ethiopia
guiarti	1	Côte d Ivoire
modestus	3	France, Russia
neavei	4	Senegal, South Africa
nigripes	1	Central African Republic
perexiguus	1	Israel
perfuscus group	3	Central African Republic, Senegal
pipiens[a]	7	South Africa, Egypt, Israel, Romania, Czechland, Bulgaria[b]
poicilipes	29	Senegal
pruina	1	Central African Republic
quinquefasciatus[a]	7	India, Pakistan, Madagascar
scottii	1	Madagascar
theileri[a]	4	South Africa
tritaeniorhynchus[a]	3	Pakistan, India, Madagascar
univittatus[a]	51	Egypt, Israel, South Africa, Madagascar
vishnui[a] group	6	India, Pakistan
weschei	1	Central African Republic
sp.	3	Egypt, Algeria, Cent. African Rep.
Coquillettidia metallica	1	Uganda
microannulata	1	South Africa
richiardii	5	South Russia, Bulgaria[b]
Mansonia uniformis	1	Ethiopia
Aedes aegypti[a]	1	Madagascar
africanus	1	Central African Republic
albocephalus	35	Madagascar

Mosquitoes species	N°	Paesi
Aedes albothorax	1	Kenya
cantans	7	Slovakia, Ukraine, Bulgaria[b]
caspius[a]	1	Ukraine
circumluteolus	2	South Africa, Madagascar
excrucians	1	Ukraine
juppi+caballus	1	South Africa
madagascarensis	1	Madagascar
vexans	3	Senegal, Russia
Anopheles brunnipes	1	Madagascar
coustani	1	Israel
maculipalpis	1	Madagascar
maculipennis	3	Portugal, Ukraine
subpictus	1	India
sp.	1	Madagascar
Mimomyia hispida	8	Senegal
lacustris	4	Senegal
splendens	6	Senegal
sp.	2	Senegal
Aedeomyia africana	1	Senegal
Soft ticks species		
Argas hermanni[a]	3	Egypt
Ornithodoros capensis[a]	5	Azerbaijan
Hard ticks species		
Hyalomma marginatum	5	Astrakhan, Azerbaijan
detritum	1	Turkmenistan
Rhipicephalus turanicus	1	Azerbaijan
muhsamae	1	Central African Republic
Amblyomma variegatum	1	Central African Republic
Dermacentor marginatus[a]	1	Moldavia

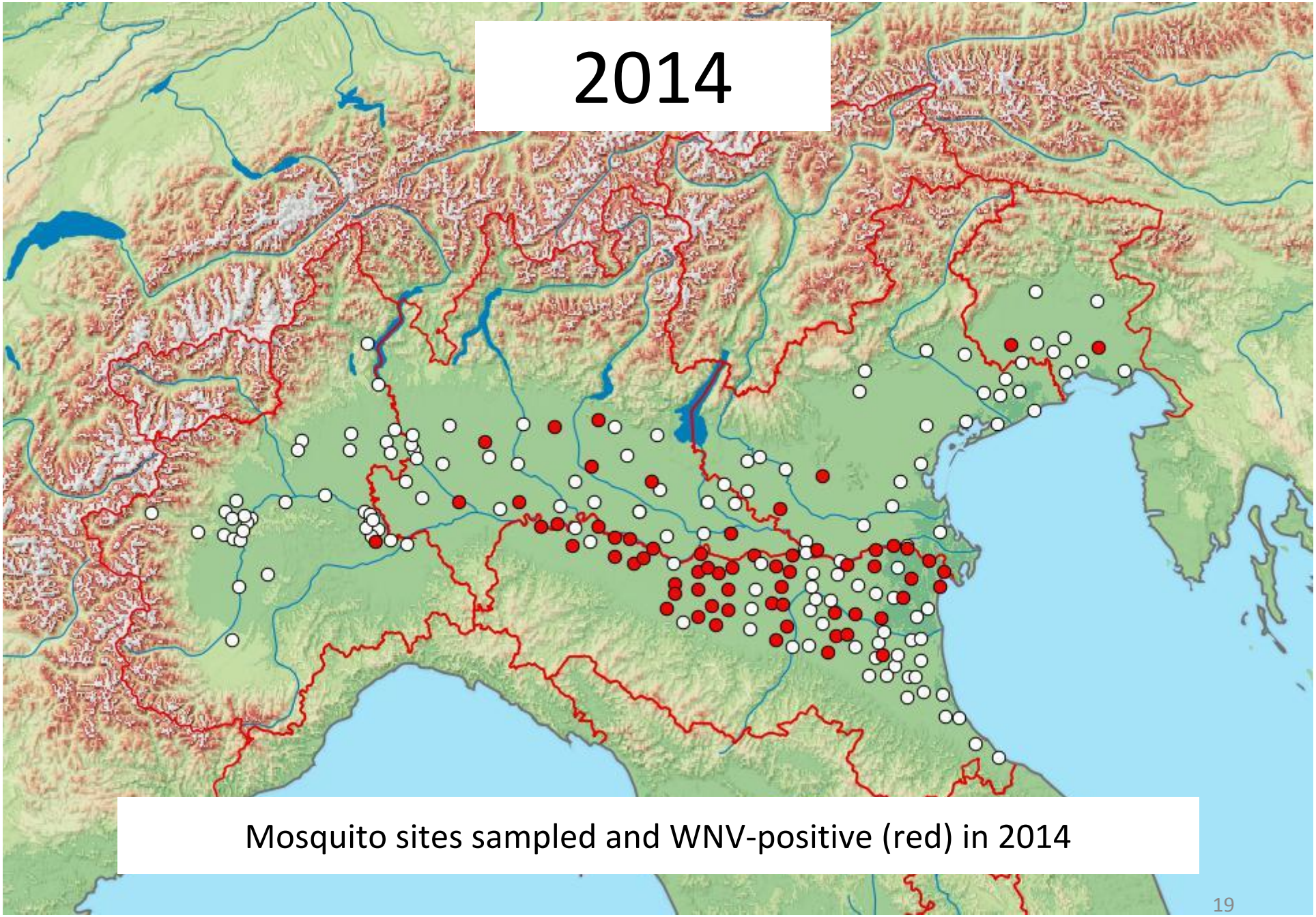
Figure 2. Map of Italy showing the areas where different WNV strains were detected in the period from September 2008 to August 2013. WNV lineage 1 strains are indicated in blue; WNV lineage 2 strains are indicated in red.



Barzon *et al. Int. J. Environ. Res. Public Health* ***2013, 10***



Mosquito sites sampled and WNV-positive (red) in 2013

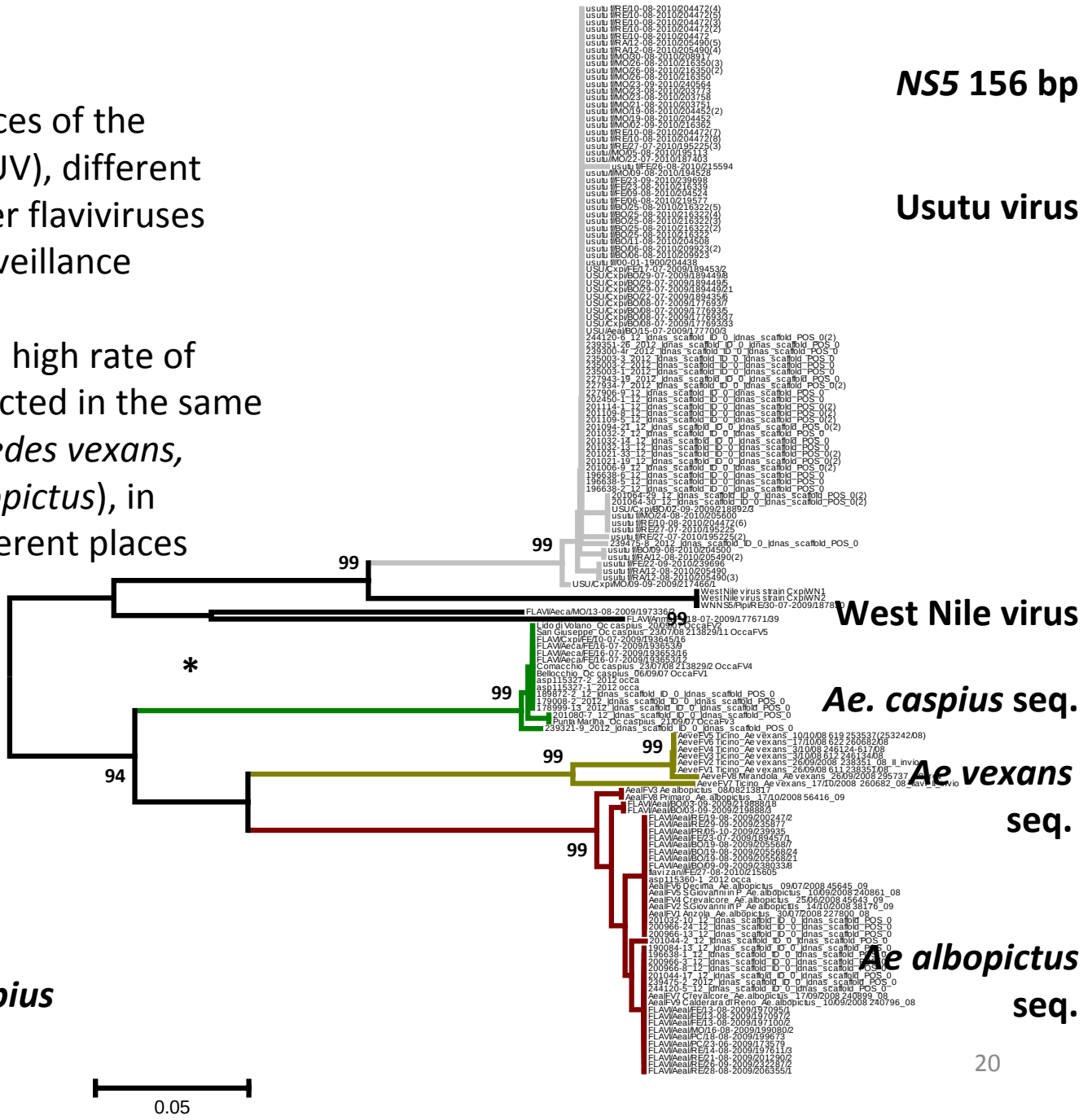


Mosquito sites sampled and WNV-positive (red) in 2014

Unespected results

In addition to the sequences of the surveyed virus (WNV, USUV), different sequences related to other flaviviruses were detected during surveillance

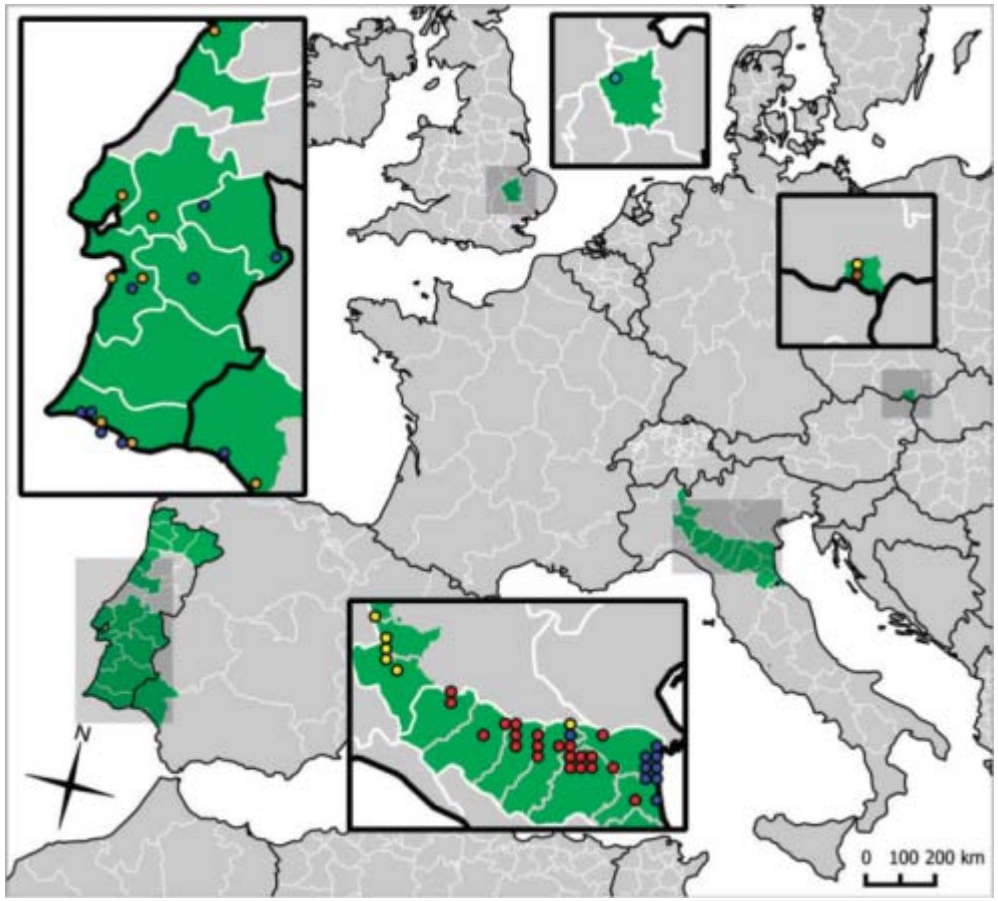
Groups of sequences with high rate of identity were mainly detected in the same species of mosquitoes (*Aedes vexans, Aedes caspius, Aedes albopictus*), in different years and in different places strongly suggest the presence of viruses not yet discovered.



*** Two sequences *Ae. caspius***
An. maculipennis

Mosquito-only flavivirus

- Interestingly similar sequence were detected from other groups in Europe, in similar surveillance plans in different mosquito species.
- Six groups of sequences were detected
- The sequences from *Aedes albopictus* are related to a virus isolated in Japan in 2009
- Isolation of Ochlerotatus flavivirus was successful in Portugal and Spain



Calzolari et al. 2012 JGV

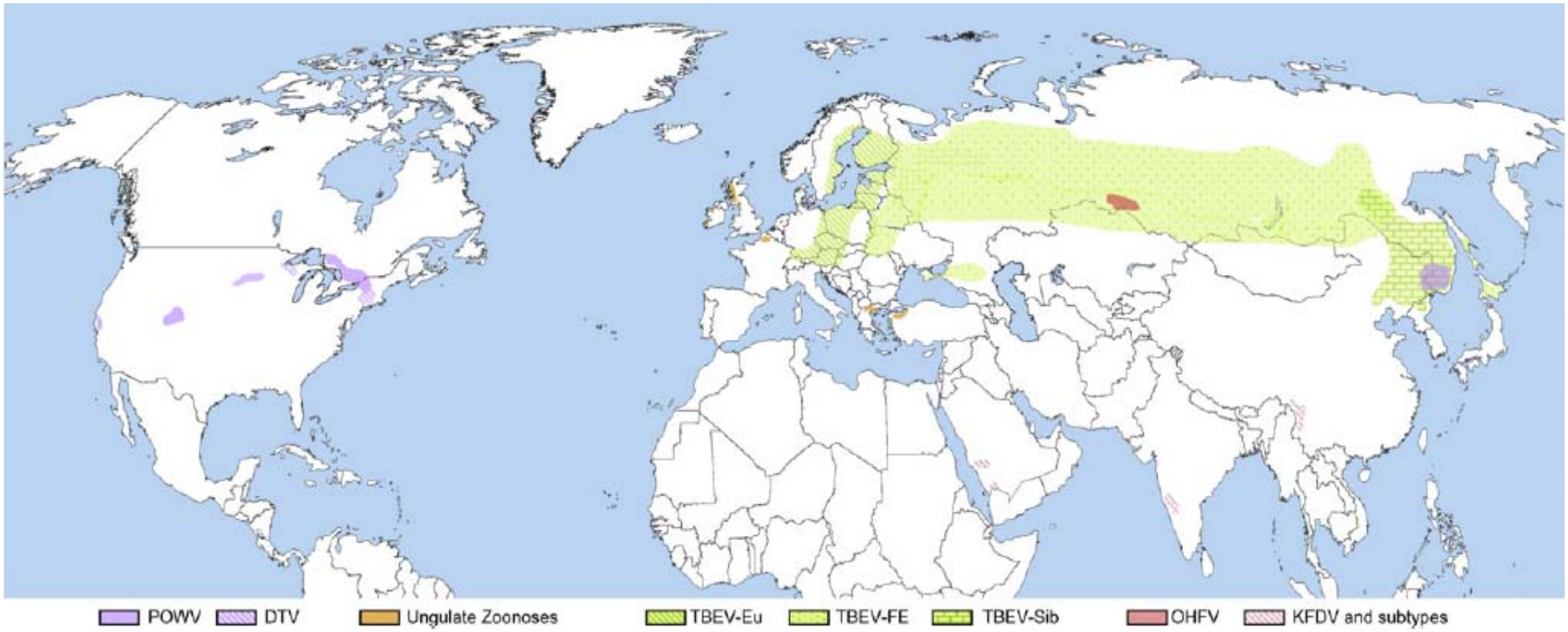
Table 2. Characteristics of the reported MOFs with the reference to the mosquito species, number, period, area and environment of detection

Virus	Mosquito species	No. detections (in GenBank)	Collection period	Collection years	Country	Collection area	Environment
Aedes flavivirus	*Aedes albopictus*	32 (29)*	June–October	2008, 2009, 2010	Italy	Pianura Padana	Floodplain
Ochlerotatus flavivirus	*Aedes caspius/detritus Culex pipiens/perexiguus/theileri*	33 (22)†	March–October	2007, 2008, 2009, 2010	Italy, Portugal, Spain	Lidi Ferraresi, Algarve, Alentejo, Andalusian	Inland and tidal wetland
Aedes vexans flavivirus	*Aedes vexans*	9 (9)‡	July–November	2008, 2009	Czech Republic, Italy	Pianura Padana, South Moravia	Inland wetland
Czech *Aedes vexans* flavivirus	*Aedes vexans*	4 (4)§	August	2009	Czech Republic	South Moravia	Pond
Culex theileri flavivirus	*Culex theileri*	15 (9)‖	March–October	2007, 2008, 2009, 2010	Portugal, Spain	Alentejo, Algarve, Centro, Ribatejo Andalusian	Inland and tidal wetland
Aedes cinereus flavivirus	*Aedes cinereus*	17¶	June–July	2010	UK	Cambridgeshire	Inland wetland

Conclusioni

- E’ possibile l’introduzione di nuovi flavivirus in Nord Italia, alcuni dei più pericolosi per l’uomo possono essere trasemessi dalla zanzara tigre
- Esiste un grande varietà di flavivirus, non necessariamente patogeni, già presente sul nostro territorio
- WNV ed USUV circolano regolarmente in Nord Italia
- La sorveglianza entomologica è in grado di rilevare la presenza ed il periodo di circolazione dei flavivirus

Tick-transmitted Flavivirus



Flavivirus del nuovo mondo:
USA
Powassan virus
Deer Tick virus

Louping Ill
Greek goat encephalitis
Turkey sheep encephalitis

TBE: 3 sotoogruppi:
Europeo
Russo (Far East)
Siberiano

Flavivirus che causano malattie emorragiche:
Omsk Haemorragic Fever (Russia)
Kysanur Forest Disease (India)

Tick-transmitted Flavivirus- human diseases

Table 1
Major tick-borne flaviviruses of medical significance including principal tick vector and vertebrate host(s)

Virus (Abbreviation)	Subtypes	Principal Vector	Intermediate Host(s)	Case Fatality Rate[b]
Tick-borne encephalitis virus (TBEV)	European subtype	*Ixodes ricinus*	Field mice, other rodents	0.5%–2%
	Far Eastern subtype	*I persulcatus* (also *Haemaphysalis concinna*)		5%–20%
	Siberian subtype	*I persulcatus* (also *H. concinna*)		1%–3%
Omsk hemorrhagic fever virus (OHFV)		*Dermacentor reticulatus*	Voles, muskrats	0.5%–3%
Kyasanur Forest disease virus (KFDV)		*H spinigera*	Rodents, shrews, birds, monkeys	2%–10%
	Alkhurma hemorrhagic fever virus (AHFV)	Unknown	Unknown (suspect goats, sheep and/or camels)	25%
Powassan virus (POWV)		*I cookei* (North America), *H longicornis* (East Asia)	Groundhogs, woodchucks, foxes, squirrels, skunks	20%
	Deer tick virus (DTV)	*I scapularis*	White-footed mice	Unknown
Louping ill virus (LIV)[a]	Greek goat encephalitis virus (GGEV)	*I ricinus*	Mountain hares, sheep, goats, grouse	Very rare
	Turkish sheep encephalitis virus (TSEV)			
	Spanish sheep encephalitis virus (SSEV)			

Tick Borne Encephalitis

piccolo Flavivirus (WN, DengueV, YFV, JEV)

1 filamento RNA positivo, racchiuso da un capside composto da una proteina (proteinaC) ed un envelope di due proteine (proteina E e prM/M) associate alla membrana.

3 sottogruppi che cross-reagiscono sierologicamente: Europa e Paesi Baltici; Russia; Siberia orientale

L'uomo si infetta con la puntura di una zecca infetta (99% dei casi), ma solo 1% dei casi sviluppa una encefalite grave.

E stata dimostrata anche la trasmissione tramite il consumo di latte di capra non pastorizzato (Slovenia, Ungheria, Repubblica ceca)

Ixodes ricinus: zecca dei boschi

TICK-BORNE ENCEPHALITIS

TBE Upsurge in Northern Italy

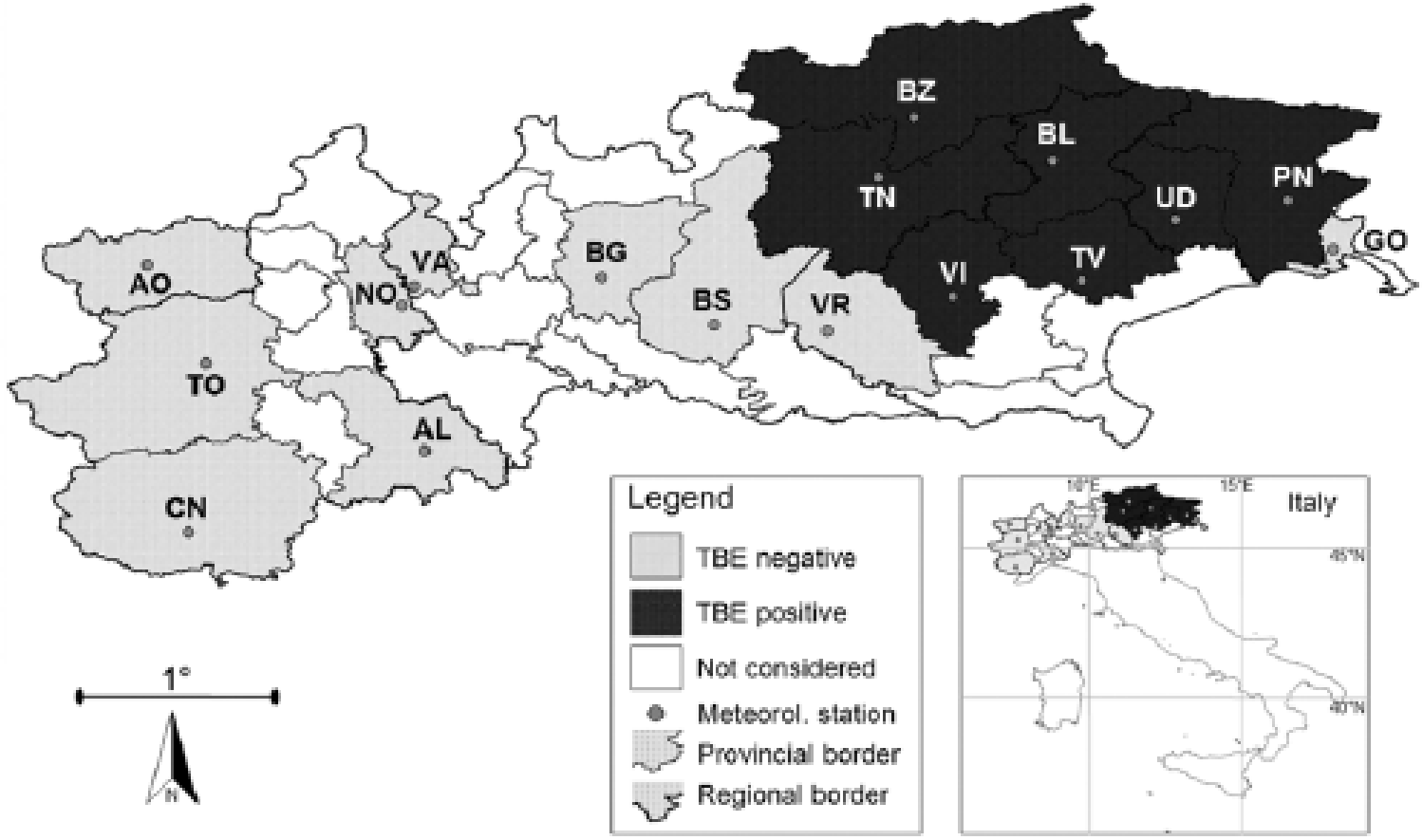


Figure 1. TBE-positive and TBE-negative provinces in northern Italy. (AL = Alessandria; AO = Aosta; BG = Bergamo; BL = Belluno; BS = Brescia; BZ = Bolzano; CN = Cuneo; GO = Gorizia; NO = Novara; PN = Pordenone; TN = Trento; TO = Torino; TV = Treviso; UD = Udine; VA = Varese; VI = Vicenza; VR = Verona).
doi:10.1371/journal.pone.0004336.g001

piccoli roditori *Apodemus e Clethrionomys* :

- ospiti con <u>viremia di una certa durata</u> e con titoli virali elevati
- un numero sufficiente di nuovi ospiti suscettibili

ospiti di grosse dimensioni (caprioli, cinghiali, lepri):

- mantenimento di un elevato numero di zecche nell'ambiente
- viremia di breve durata o inesistente

Grazie per l’attenzione

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