

Update Session: Usutu virus



WHO Collaborating Centre for Arbovirus and Haemorrhagic Fever Reference and Research, Hamburg, Germany
National Reference Centre for Tropical Diseases
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***The Triumph of Death* (1562) by Pieter Bruegel the Elder "... the plague as horrific onslaught of forces of darkness on mankind." [R. Oppenheim]**





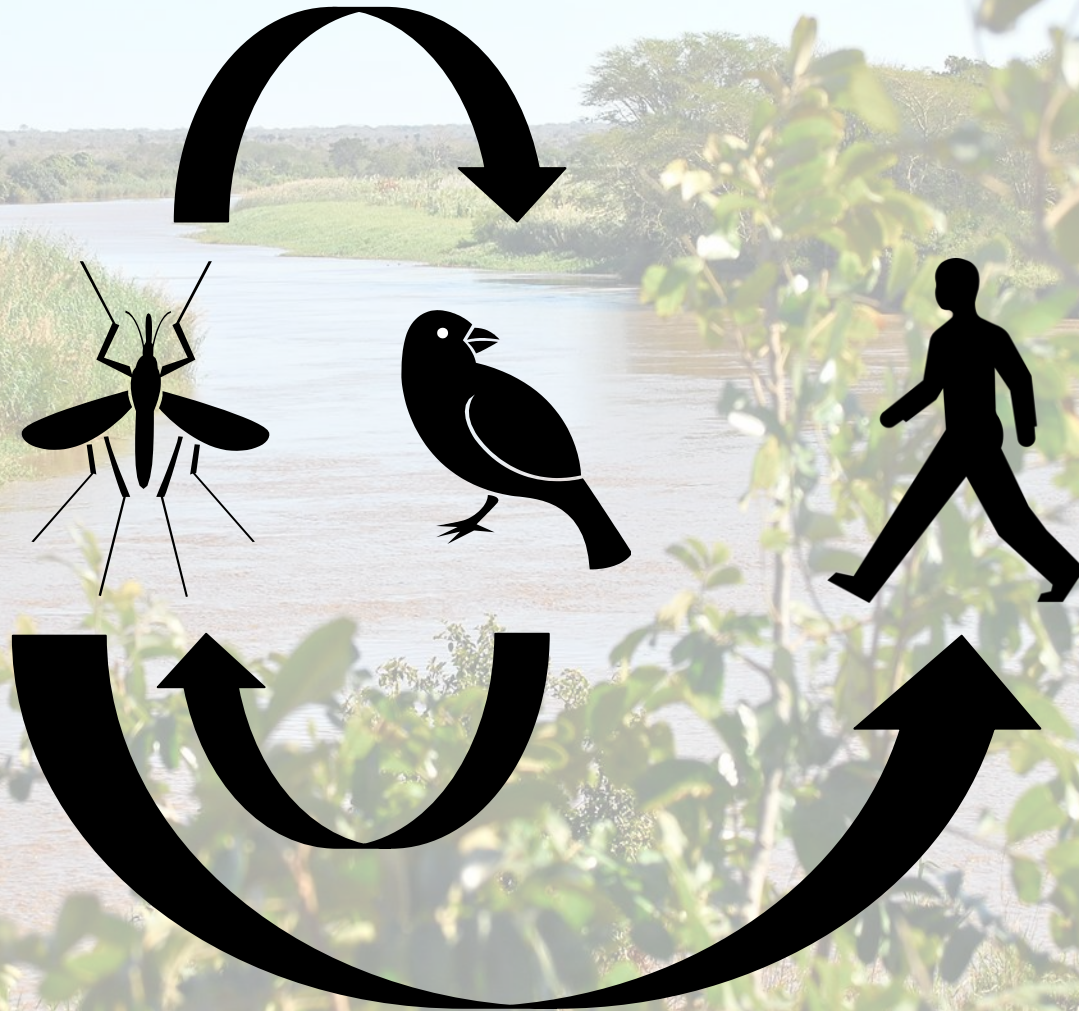
Monrovia, Liberia, 26th August 2014

Usutu virus was first isolated in 1959 from *Culex neavei* mosquitoes collected in Ndumo, South Africa.

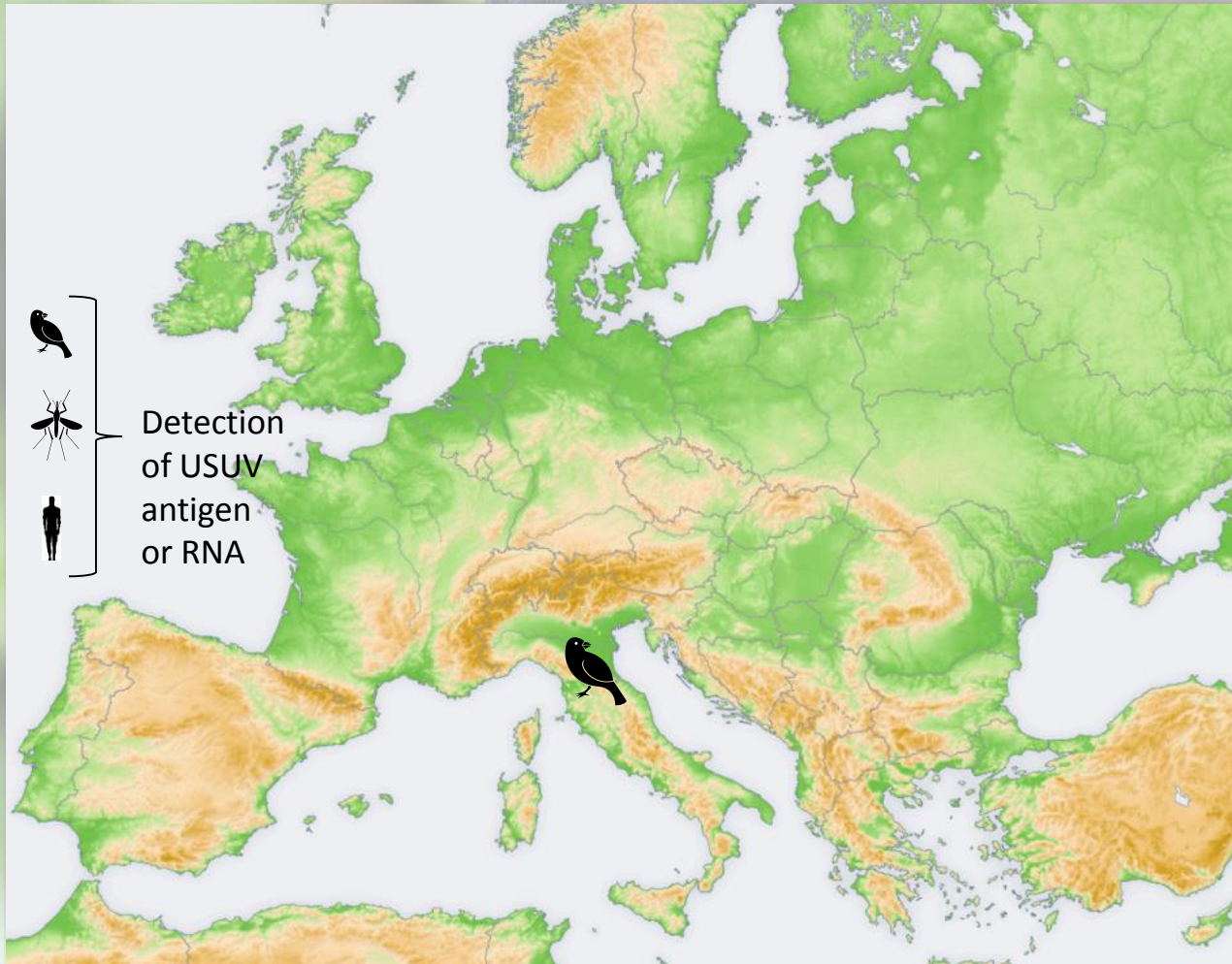


South African Institute for Medical Research

Transmission cycle Usutu virus

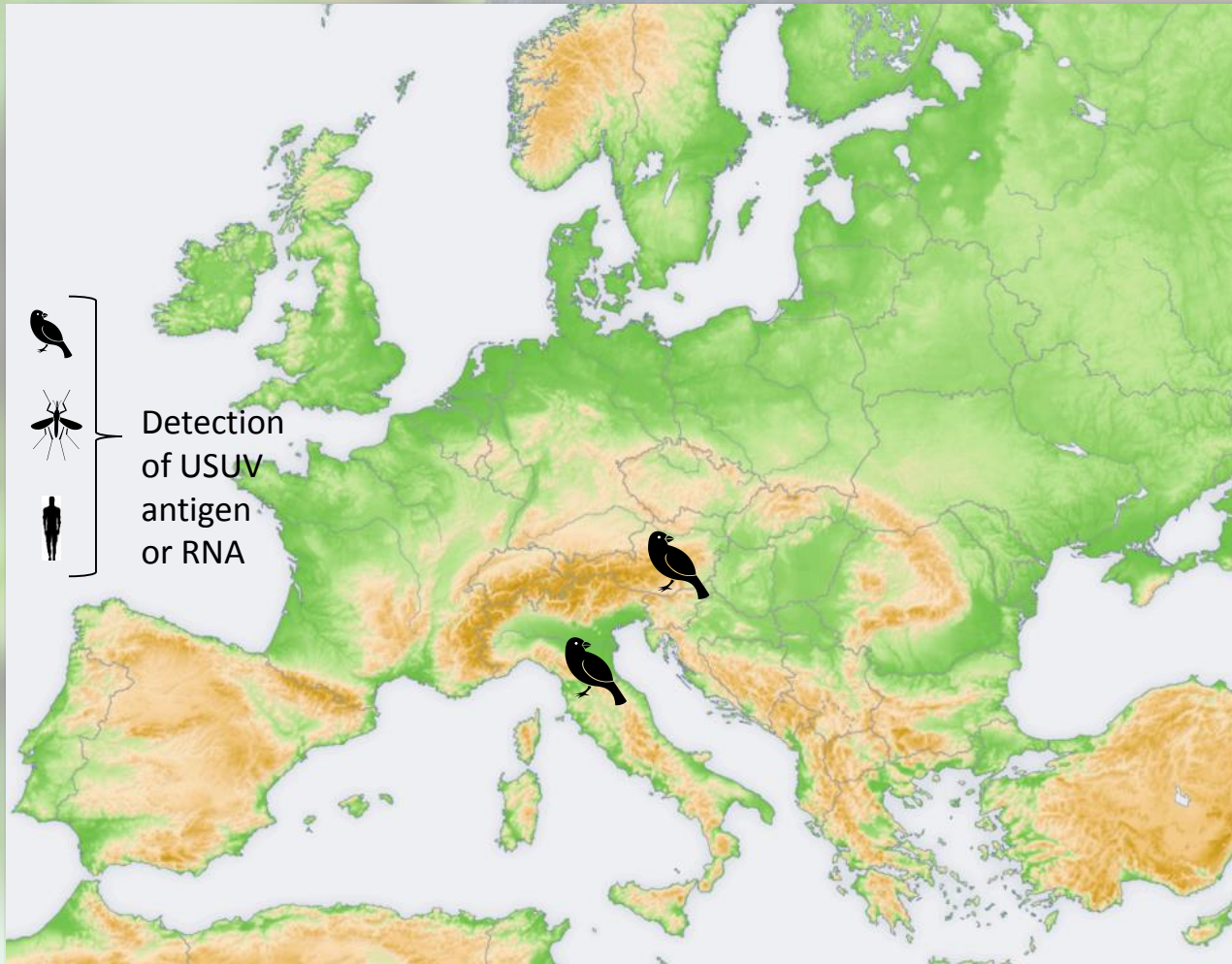


Emergence of Usutu virus in Europe



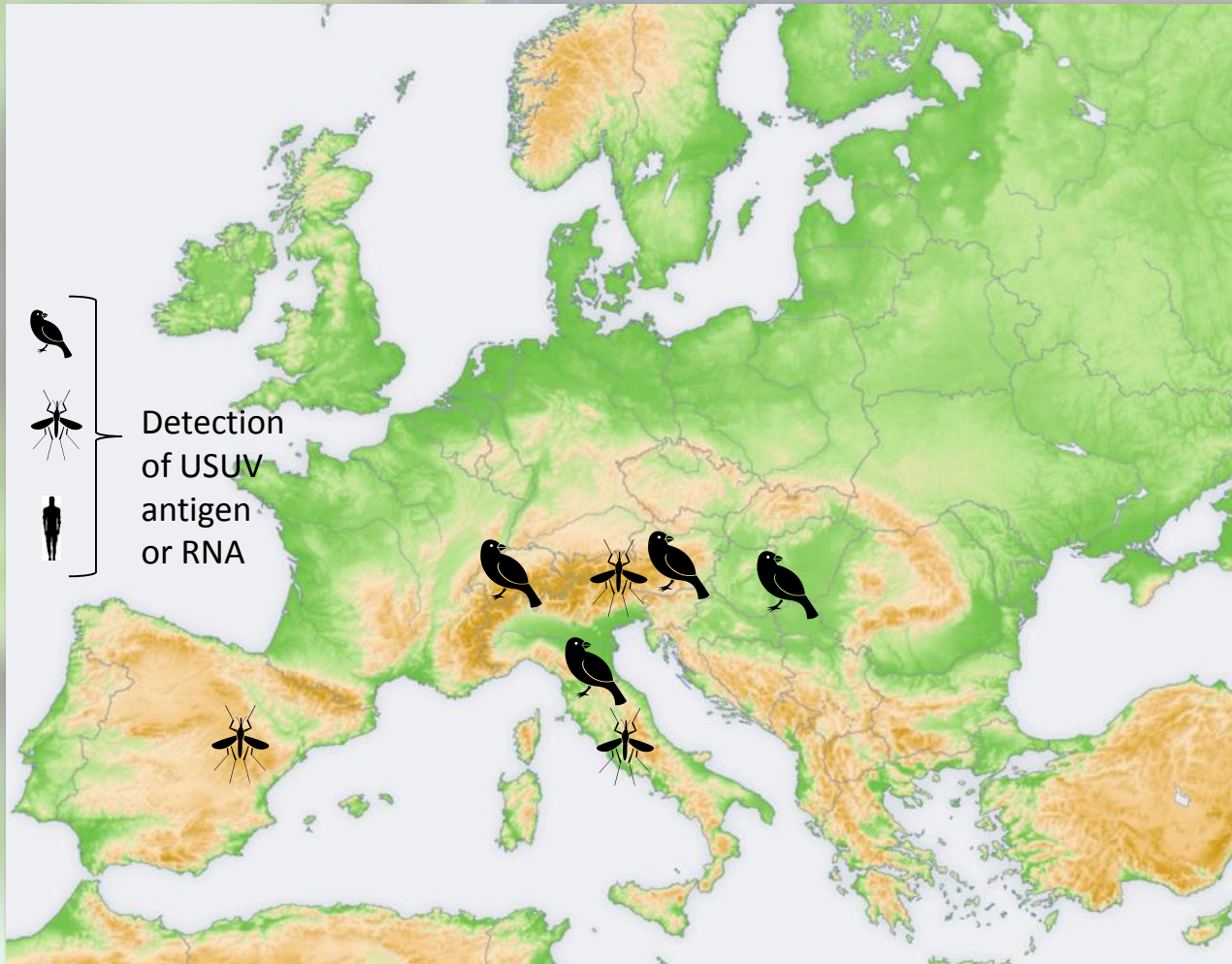
- Usutu virus was first isolated in 1959 from *Culex neavei* mosquitoes collected in Ndumo, South Africa.
- 1996: Usutu virus detected in dead black birds from Tuscany, Italy.

Emergence of Usutu virus in Europe



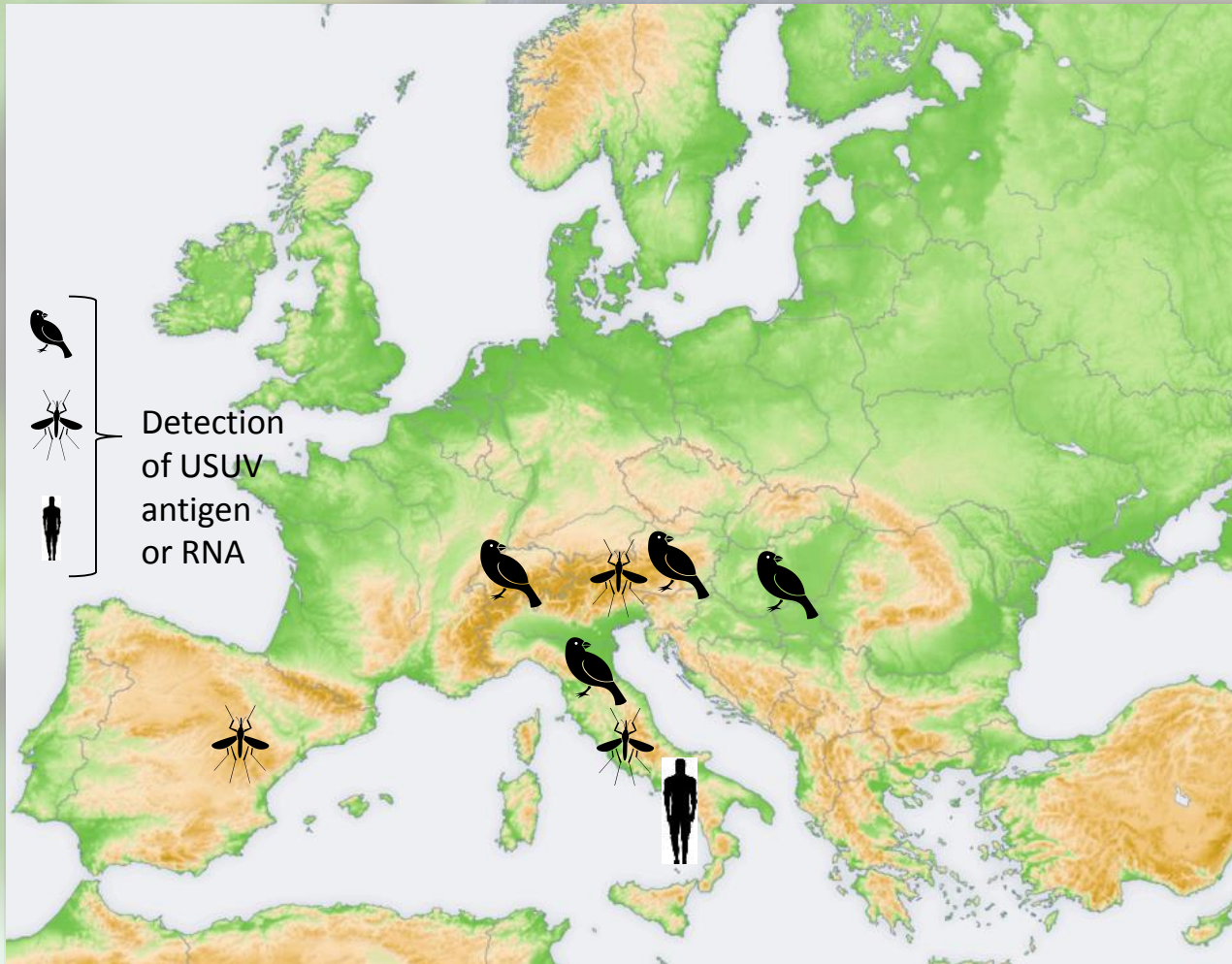
- 1996: Usutu virus detected in dead black birds from Tuscany, Italy.
- 2001: Epizootic emergence of Usutu virus in wild and captive birds, Vienna, Austria.

Emergence of Usutu virus in Europe



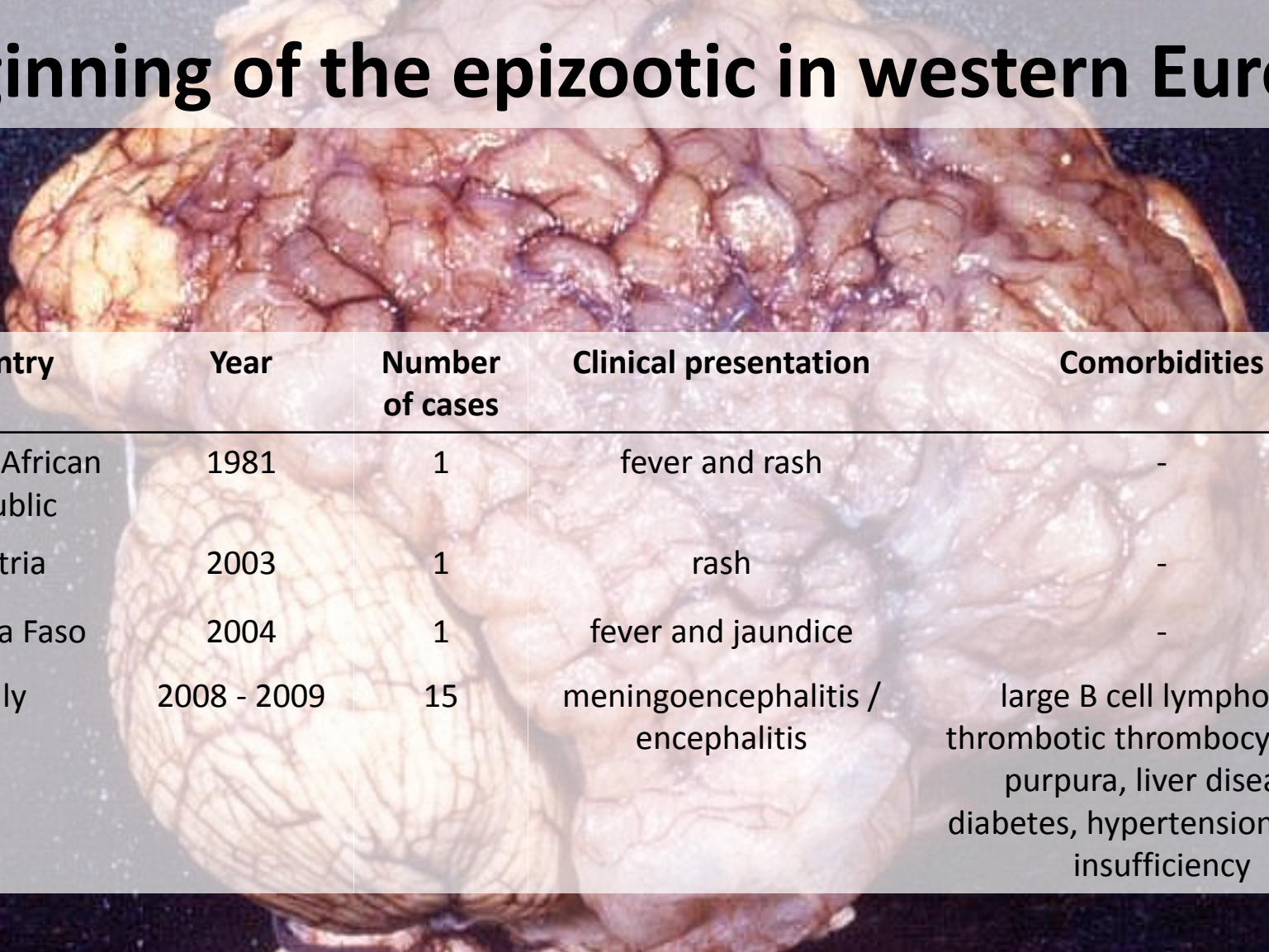
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- 2001: Epizootic emergence of Usutu virus in wild and captive birds, Vienna, Austria.
- Since 2004: Detection of Usutu virus in birds and mosquitoes from Switzerland, Italy, Hungary and Spain.

Emergence of Usutu virus in Europe



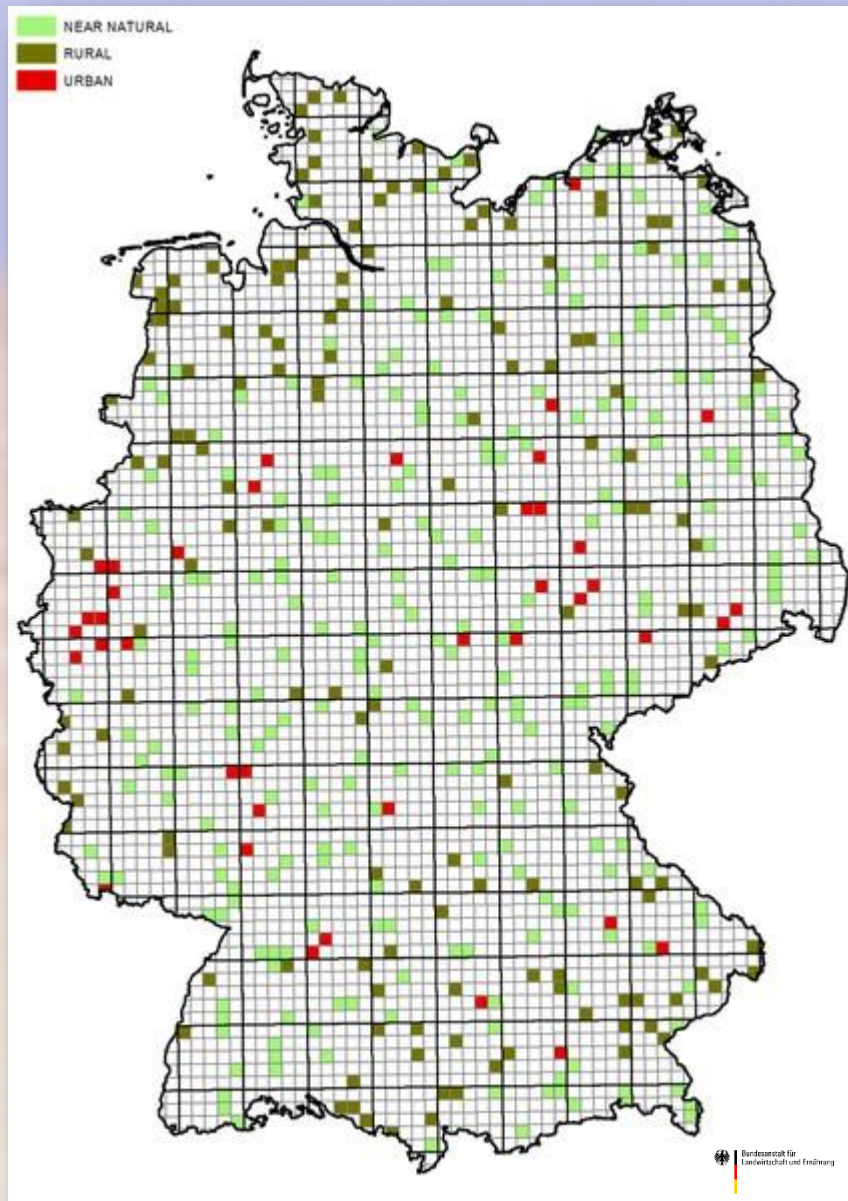
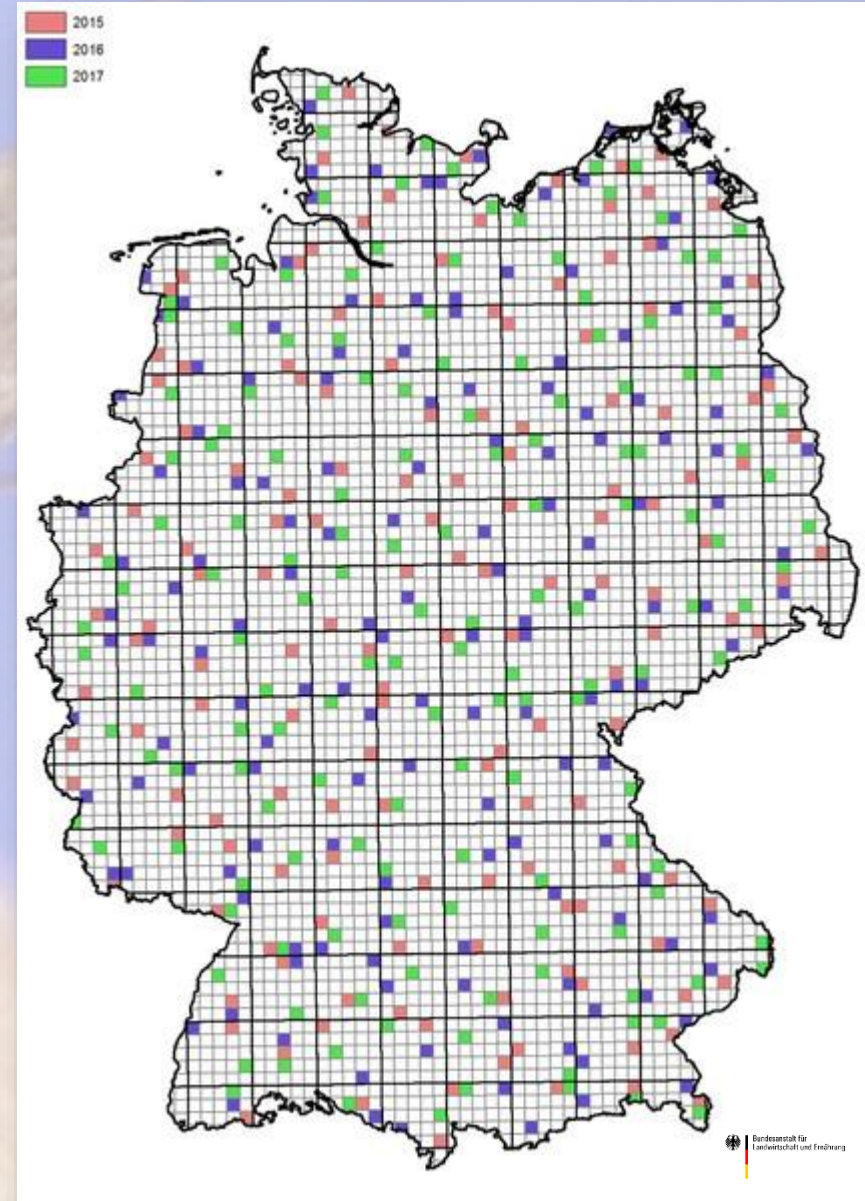
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- 2001: Epizootic emergence of Usutu virus in wild and captive birds, Vienna, Austria.
- Since 2004: Detection of Usutu virus in birds and mosquitoes from Switzerland, Italy, Hungary and Spain.
- 2009: Usutu virus was associated with neurological disorders in two immunocompromised patients from Italy.

Human Usutu virus infections until the beginning of the epizootic in western Europe



Country	Year	Number of cases	Clinical presentation	Comorbidities
Central African Republic	1981	1	fever and rash	-
Austria	2003	1	rash	-
Burkina Faso	2004	1	fever and jaundice	-
Italy	2008 - 2009	15	meningoencephalitis / encephalitis	large B cell lymphoma, thrombotic thrombocytopenic purpura, liver disease, diabetes, hypertension, mitral insufficiency

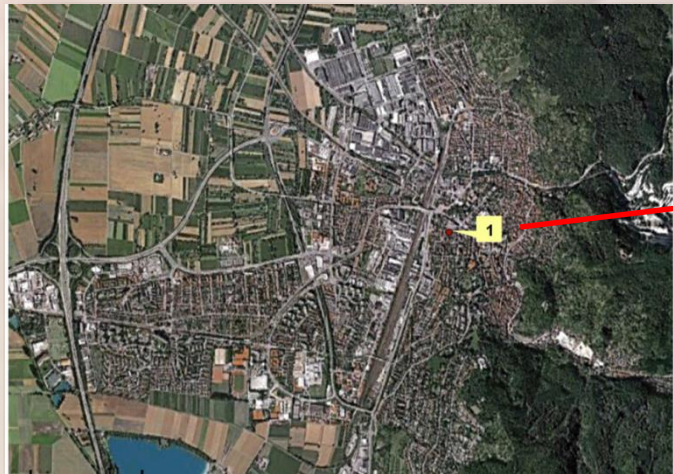
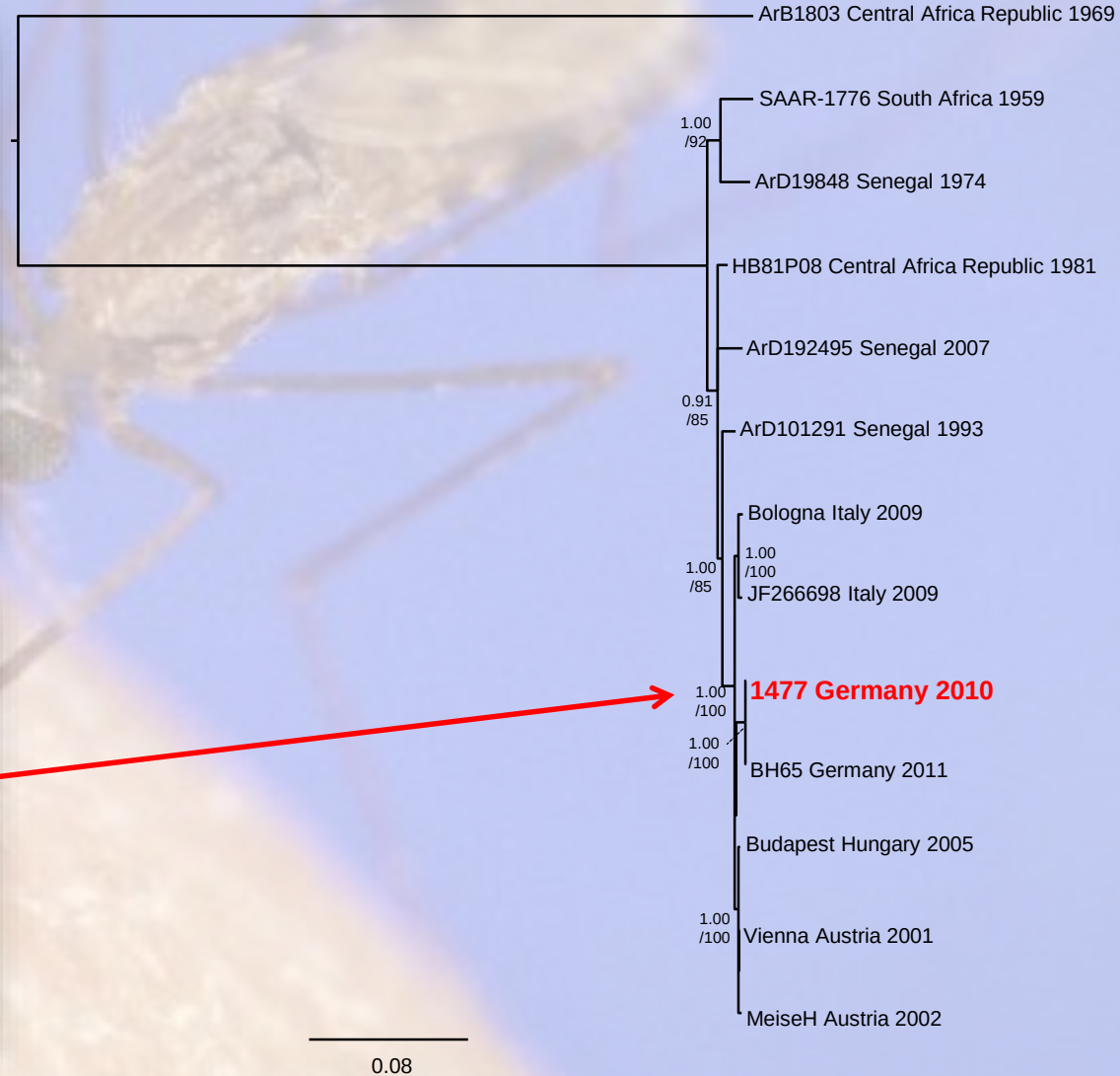
Mosquito and arbovirus surveillance program in Germany



In August 2010, Usutu virus strain 1477 was isolated from a pool of *Culex pipiens pipiens* mosquitoes that were trapped in the city of Weinheim.



trapping site „Weinheim“



The early discovery of Usutu virus in mosquitoes in 2010 followed by the recent epizootic in 2011 proof the importance and predictive value of our mosquito based monitoring program for zoonotic moboviruses.

Order	Common name	Housing	USUV RNA positive / tested (% positive)
Passeriformes	Blackbird	Wild	72 / 148 (48%)
	Common Starling	Wild	3 / 17 (17%)
	Canary	Captive	2 / 5 (40%)
	House Sparrow	Wild	1 / 1 (100%)
	European Greenfinch	Wild	0 / 10
	Fieldfare	Wild	0 / 6
	Blackcap	Wild	0 / 6
	Song Thrush	Wild	0 / 6
	European Robin	Wild	0 / 4
	Eurasian Jay	Wild	0 / 3
	Blue Tit	Wild	0 / 2
	Yellowhammer	Wild	0 / 1
	Carrion Crow	Wild	0 / 1
	Nightingale	Wild	0 / 1
Galliformes	Grey Partridge	Wild	0 / 2
Piciformes	Green Woodpecker	Wild	0 / 1
Strigiformes	Great Grey Owl	Captive	6 / 6 (100%)
Coraciiformes	Common Kingfisher	Wild	2 / 2 (100%)
Sphenisciformes	Humboldt Penguin	Captive	0 / 1
TOTAL			86 / 223 (38%)

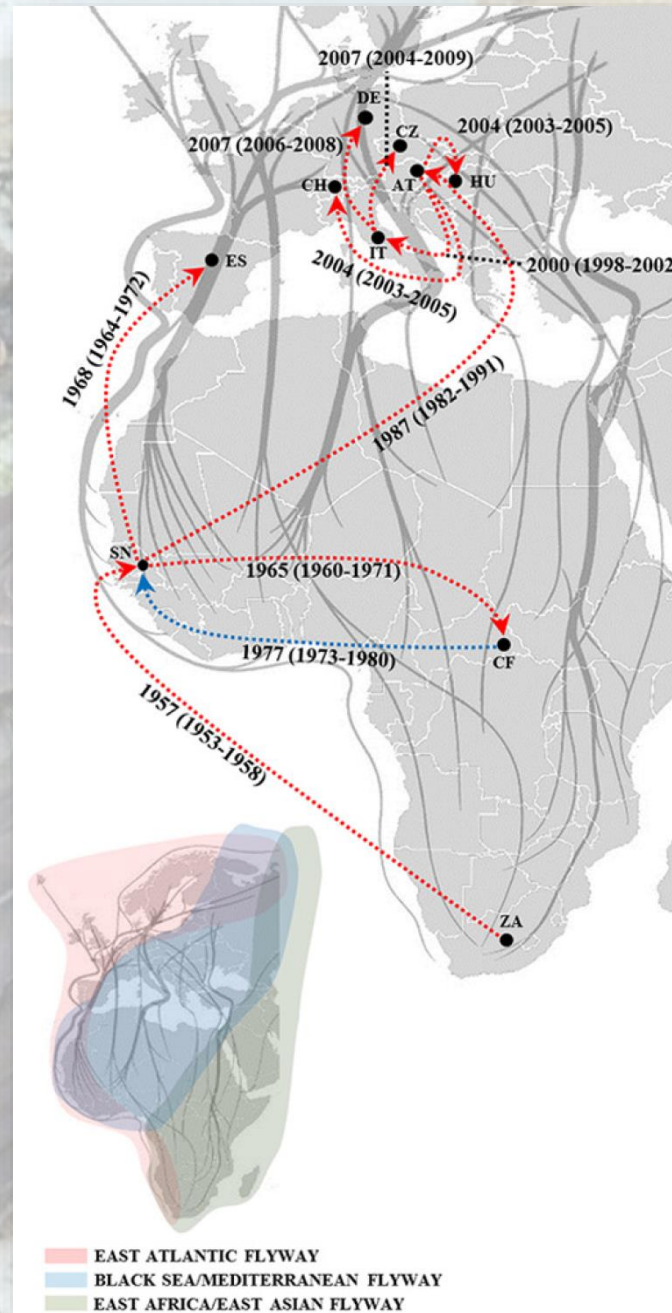


Sturnus vulgaris (common starling)

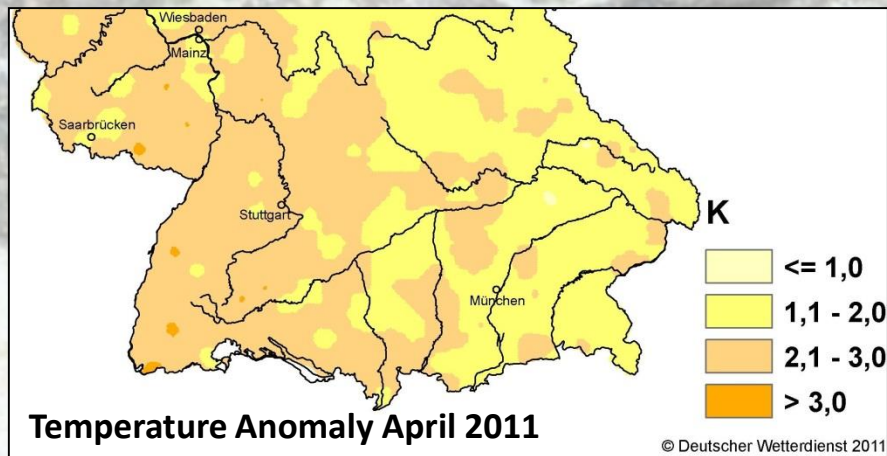
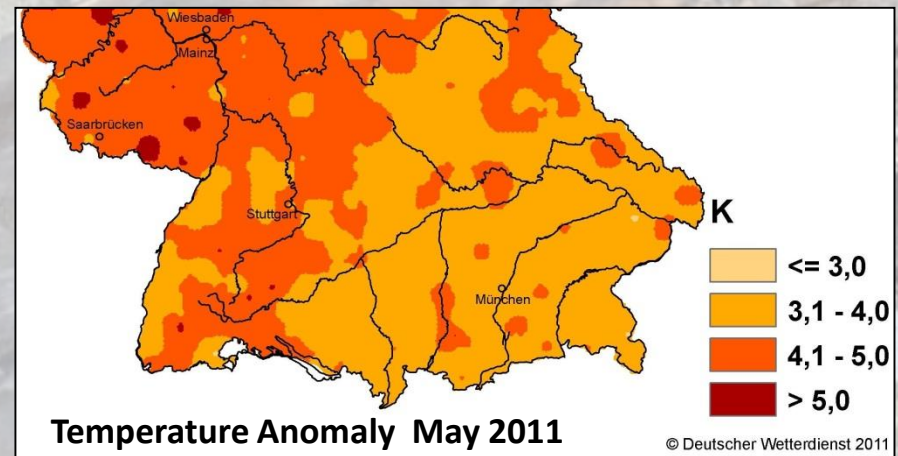
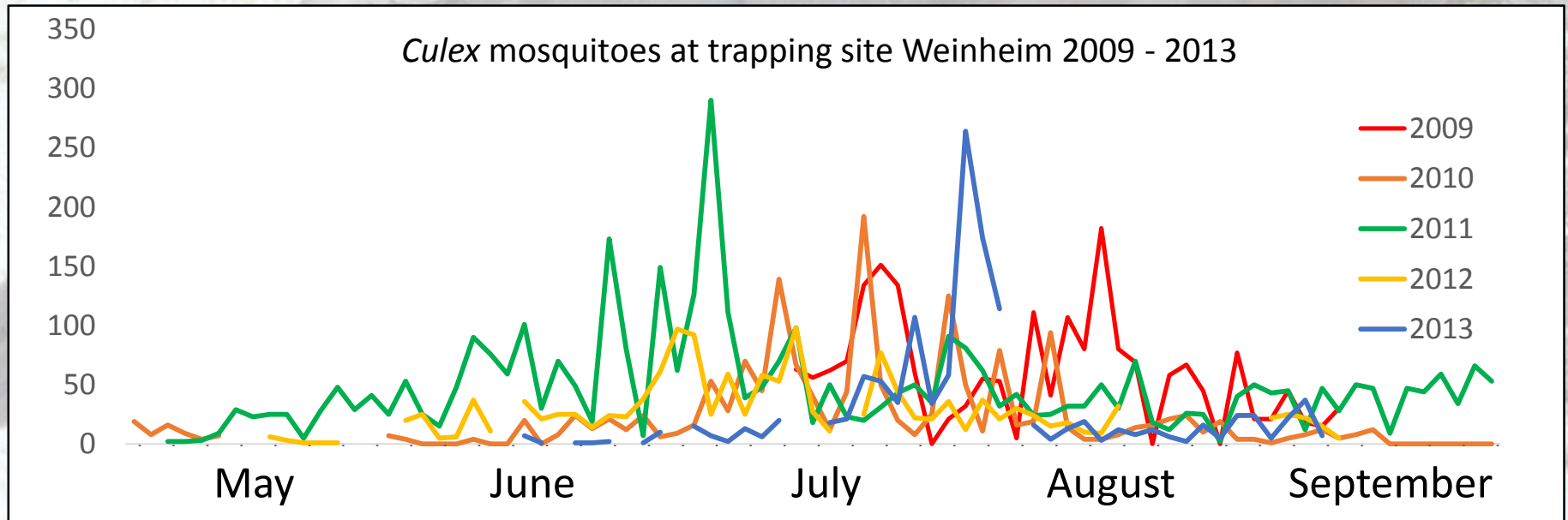


Carduelis chloris (greenfinch)

We suggest two independent introductions into Europe :



The higher average temperatures in April and May 2011 led to an increase in the number of *Culex* mosquitoes and may have contributed to the rapid spread of Usutu virus in Southwest Germany.



In 2011, the Usutu virus was transmitted to other mosquito species which are more **anthropophilic**.

2010

Culex pipiens pipiens (1)

54,321 female
mosquitoes analyzed

2011

Culex pipiens + torrentium (128)

Culex pipiens (73)

Culex torrentium (3)

***Culex modestus* (1)**

***Aedes vexans* (4)**

***Ochlerotatus cantans* (1)**

Anopheles maculipennis (1)

Anopheles claviger (1)

not determined (1)

53,230 female
mosquitoes analyzed

2012

Culex pipiens + torrentium (18)

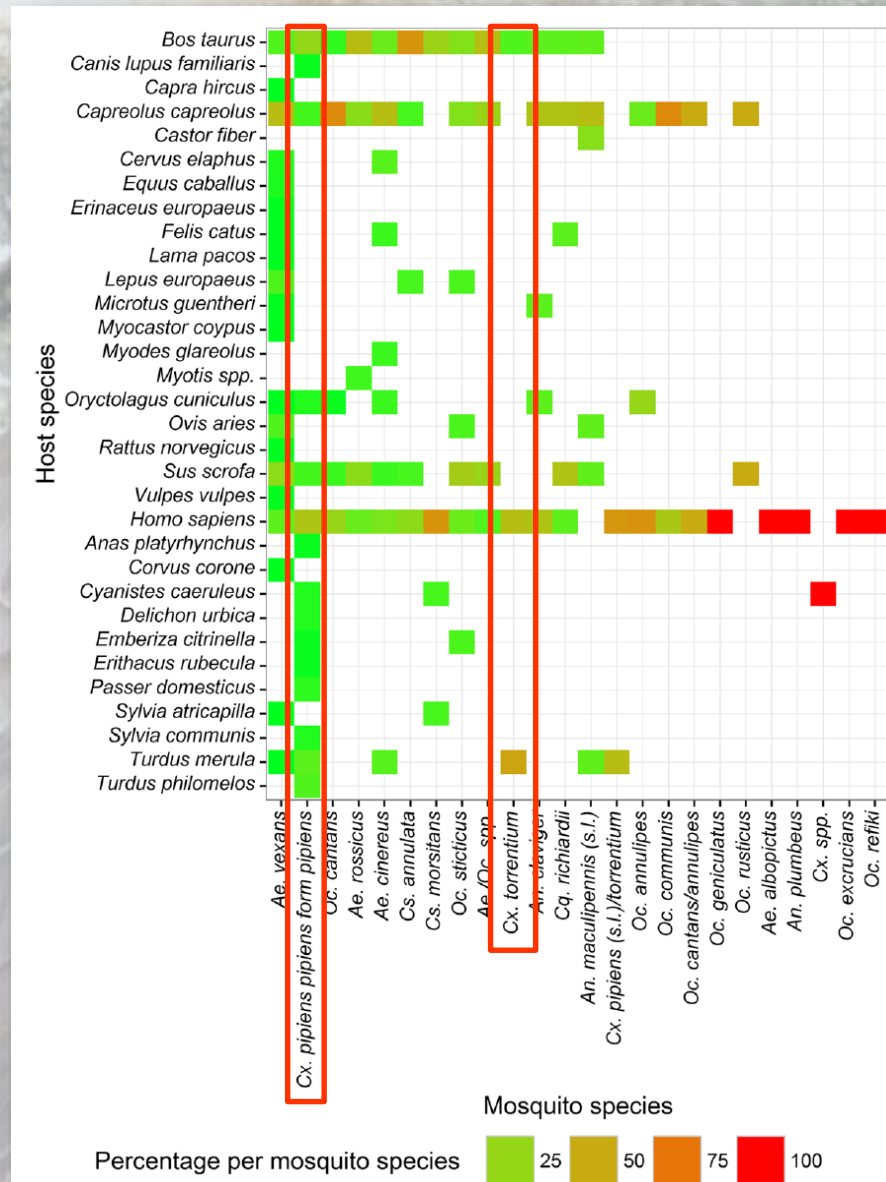
25,804 female
mosquitoes analyzed

2013

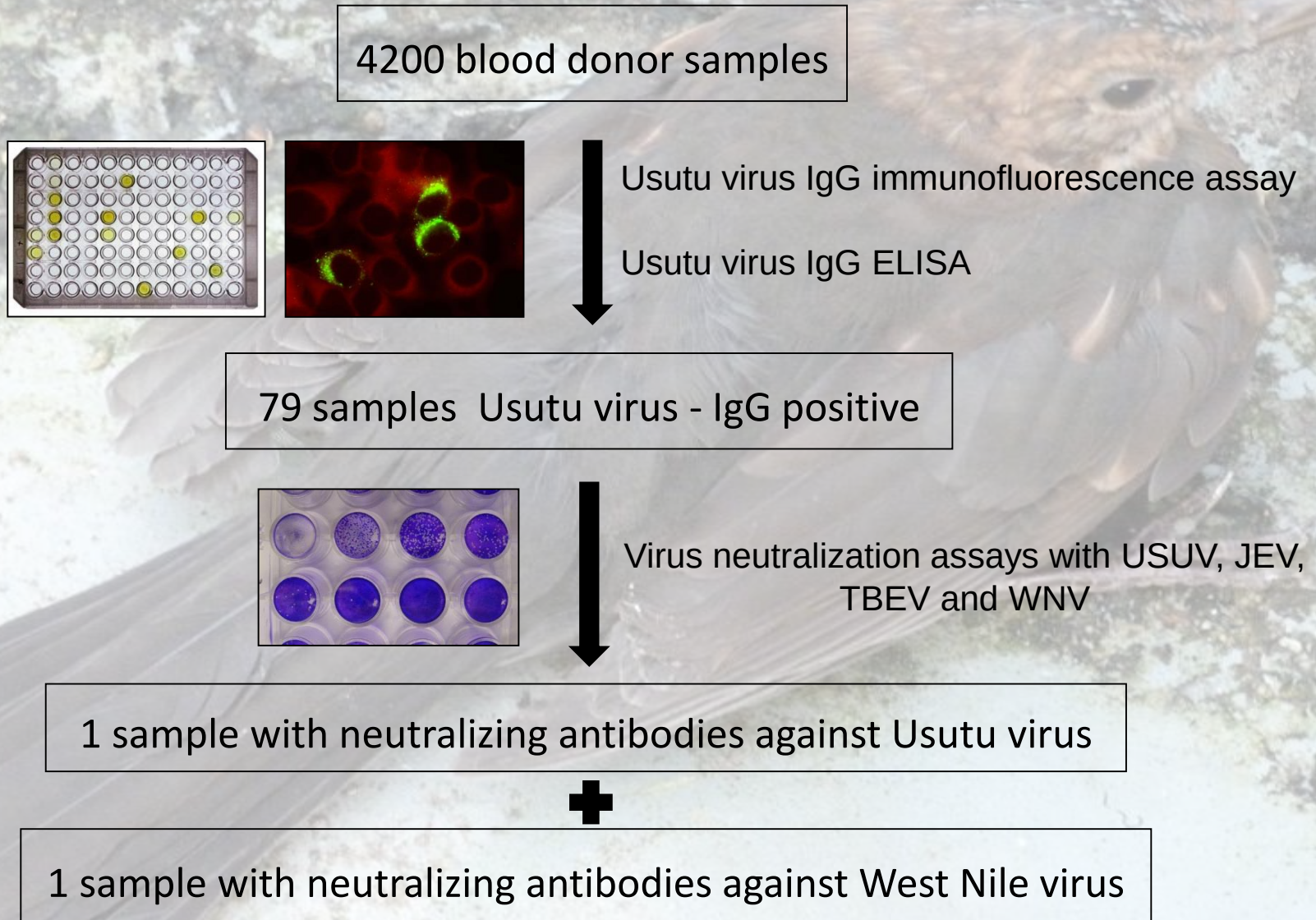
Culex pipiens + torrentium (3)

104,099 female
mosquitoes analyzed

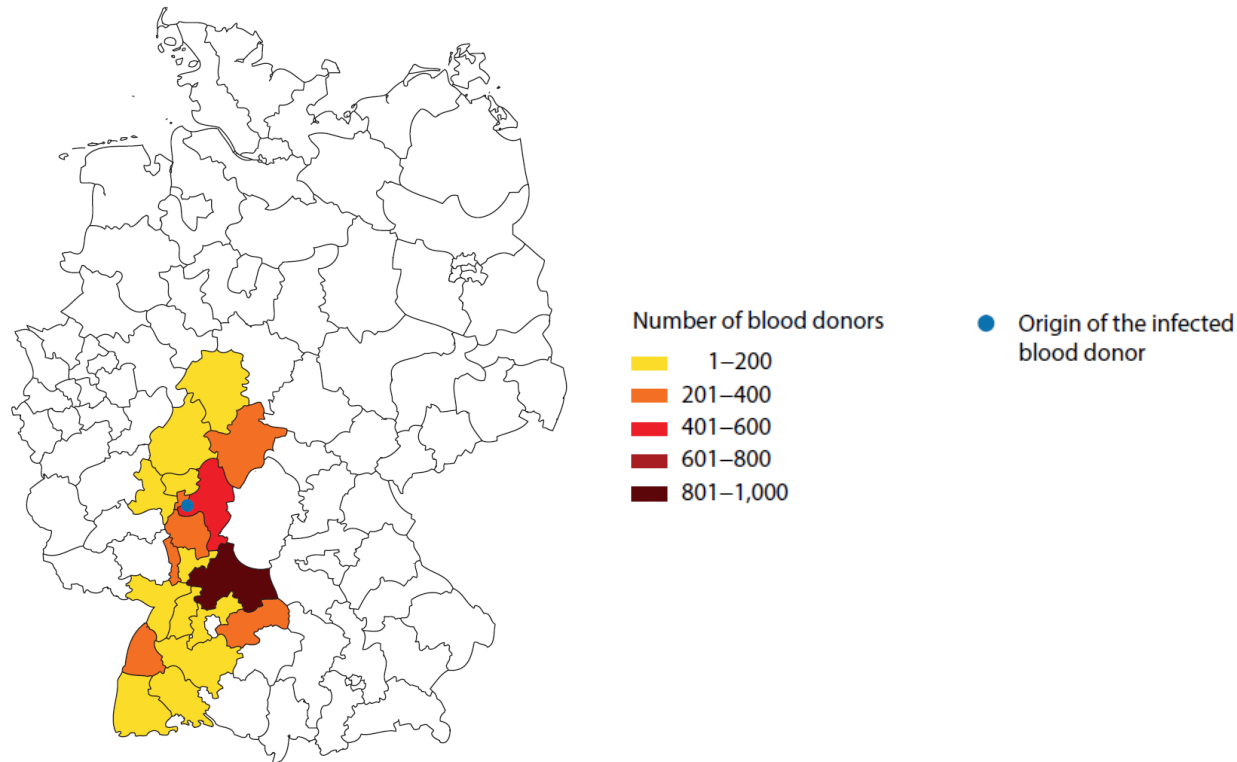
Our study on blood-fed Usutu virus vectors indicated a much broader host range compared to the classifications found in the literature, which highlights the need for such studies to further assess their vector capacity and the disease ecology.



In January 2012, 4200 samples from blood donors originating from the Usutu virus outbreak region were tested for the presence of Usutu virus-specific antibodies.



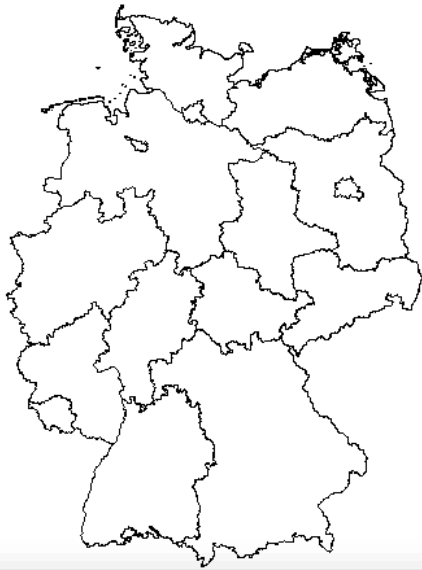
Our results corroborate the hypothesis of a pauci or asymptomatic and autochthonous Usutu virus infection of the blood donor during late summer 2011



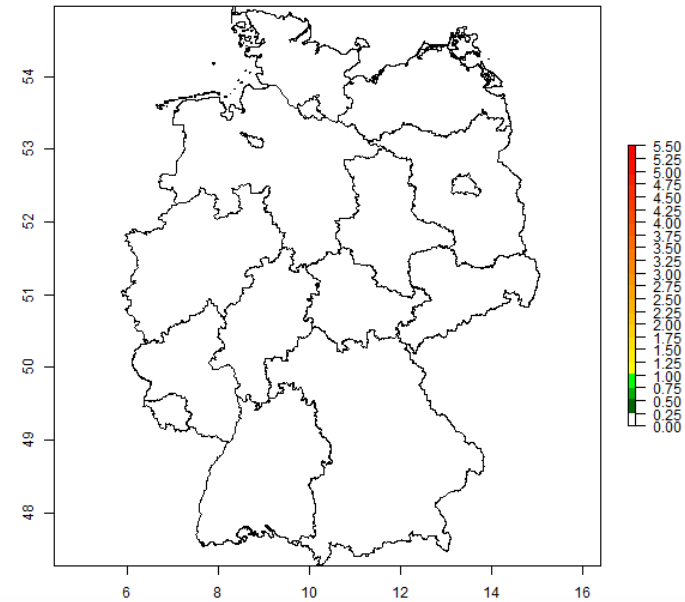
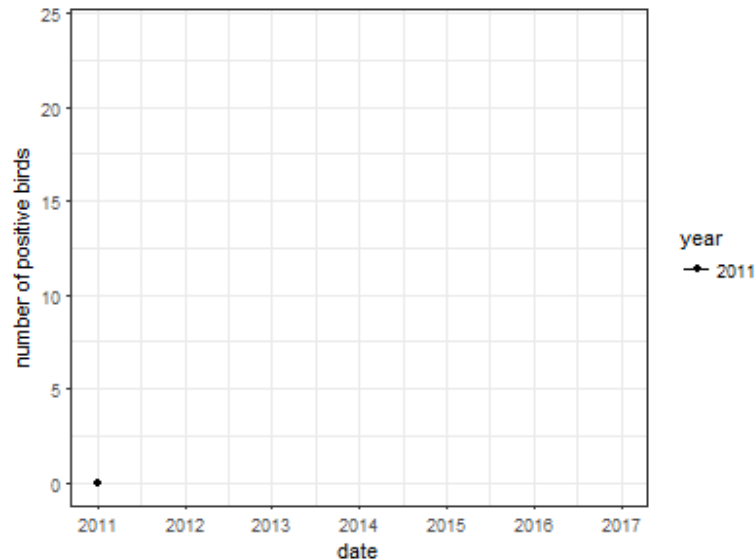
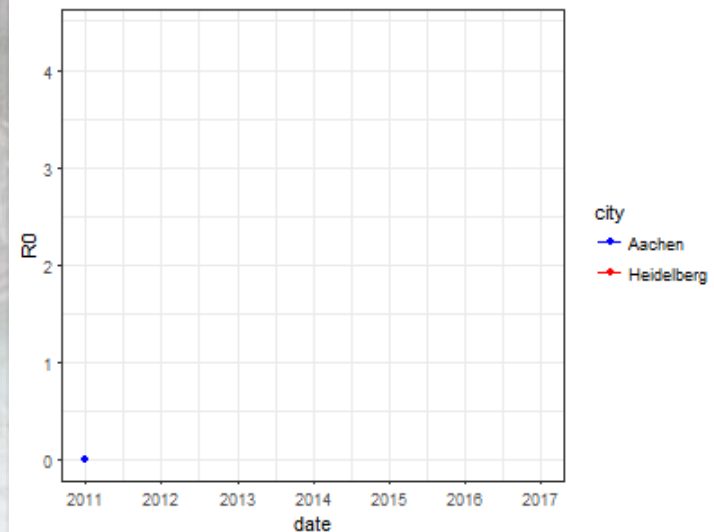
Virus	Immunofluorescence assay (IFA)												Virus neutralisation test (VNT)	
	April 2007		October 2008		October 2010		October 2011		January 2012		April 2012		January 2012	April 2012
	IgG	IgM	IgG	IgM	IgG	IgM	IgG	IgM	IgG	IgM	IgG	IgM		
Usutu	Neg	Neg	Neg	Neg	Neg	Neg	1:1,280	1:160	1:2,560	1:160	1:2,560	1:40	1:40	1:80
West Nile	Neg	Neg	Neg	Neg	Neg	Neg	1:640	1:20	1:640	1:20	1:160	1:20	Neg	Neg
Japanese encephalitis	Neg	Neg	Neg	Neg	Neg	Neg	1:2,560	Neg	1:1,280	Neg	1:640	Neg	Neg	Neg
Tick-borne encephalitis	Neg	Neg	1:80	Neg	1:160	Neg	1:1,280	Neg	1:1,280	Neg	1:1,280	Neg	Neg	1:20
Yellow fever	Neg	Neg	Neg	Neg	1:160	Neg	1:1,280	Neg	1:1,280	Neg	1:160	Neg	Neg	Neg

The spatial distribution of most of the positive cases in 2016 falls in an area with a mean basic reproduction number larger one. This high R_0 was driven by extraordinary high temperatures during September 2016, with values exceeding the long-term mean by more than 3°C .

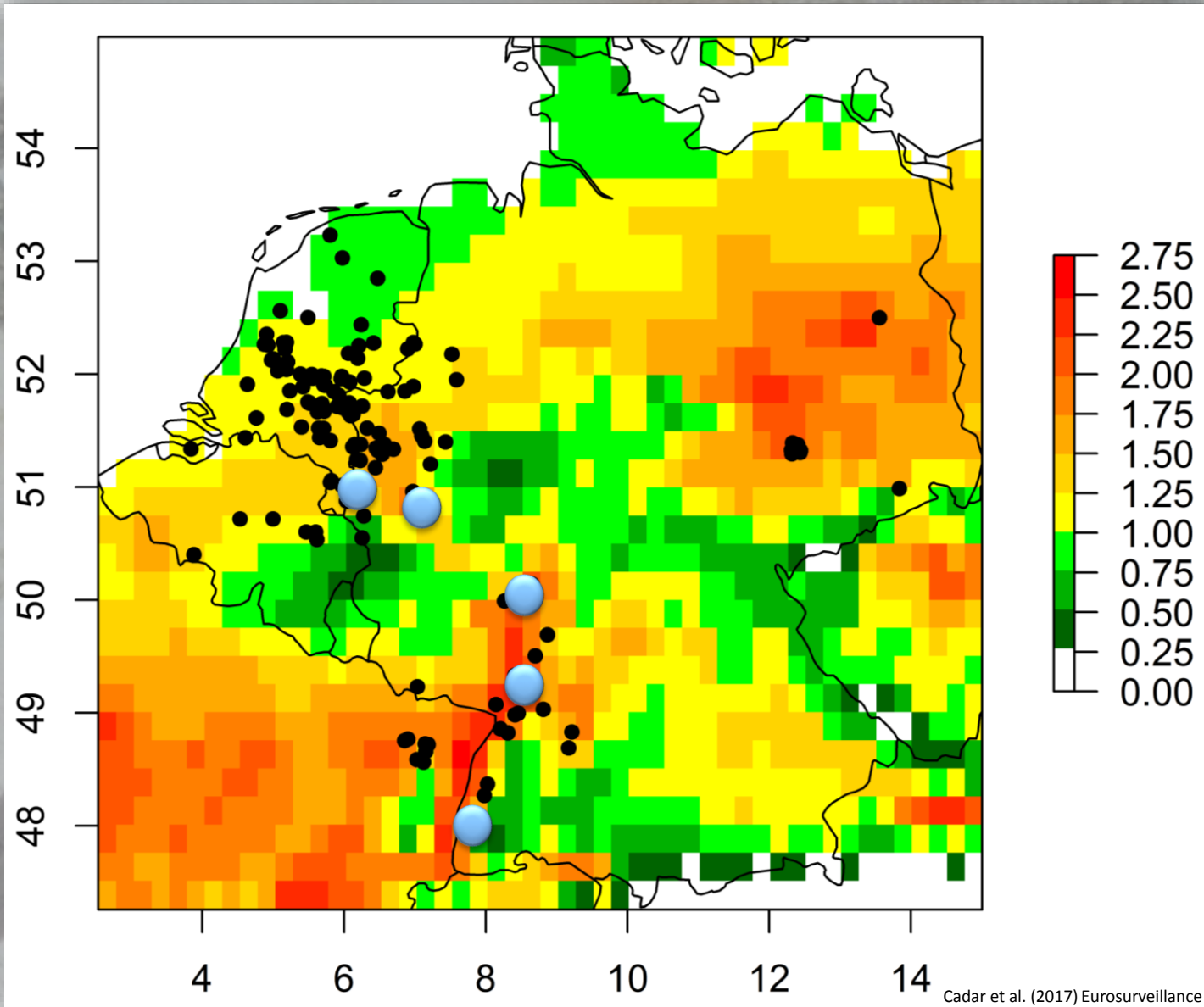
„dead bird“ Surveillance



R_0 Modell



The recent unprecedented emergence and spread of USUV in Western Europe highlights the need for a One Health approach to foster preparedness and response as we expect increased human exposure to USUV in the epizootic areas:



~16.000 blood donations, PCR, 2016



241 CSF, PCR, 2014-2016



~ 5.000 blood donations, Serologie, 2016



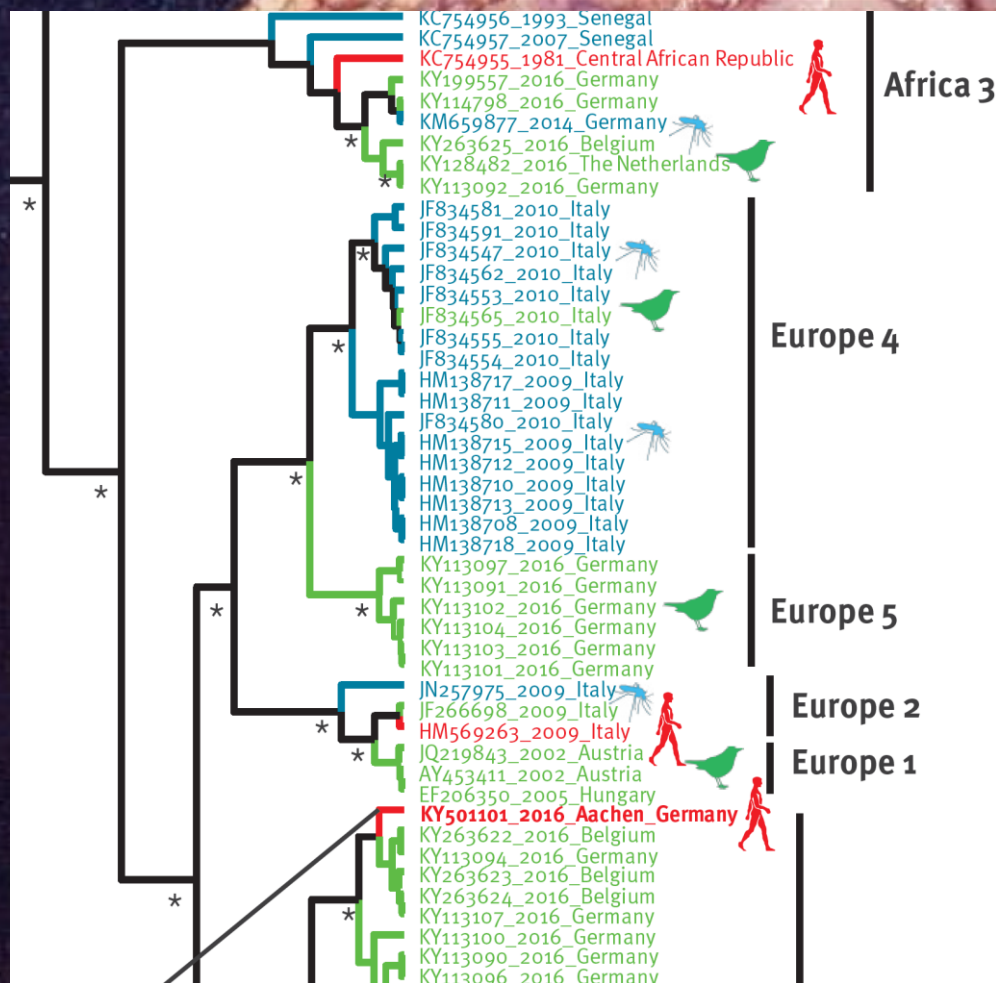
UniversitätsKlinikum Heidelberg

1997 CSF, PCR, 2011-2015



16 CSF, PCR, 2016

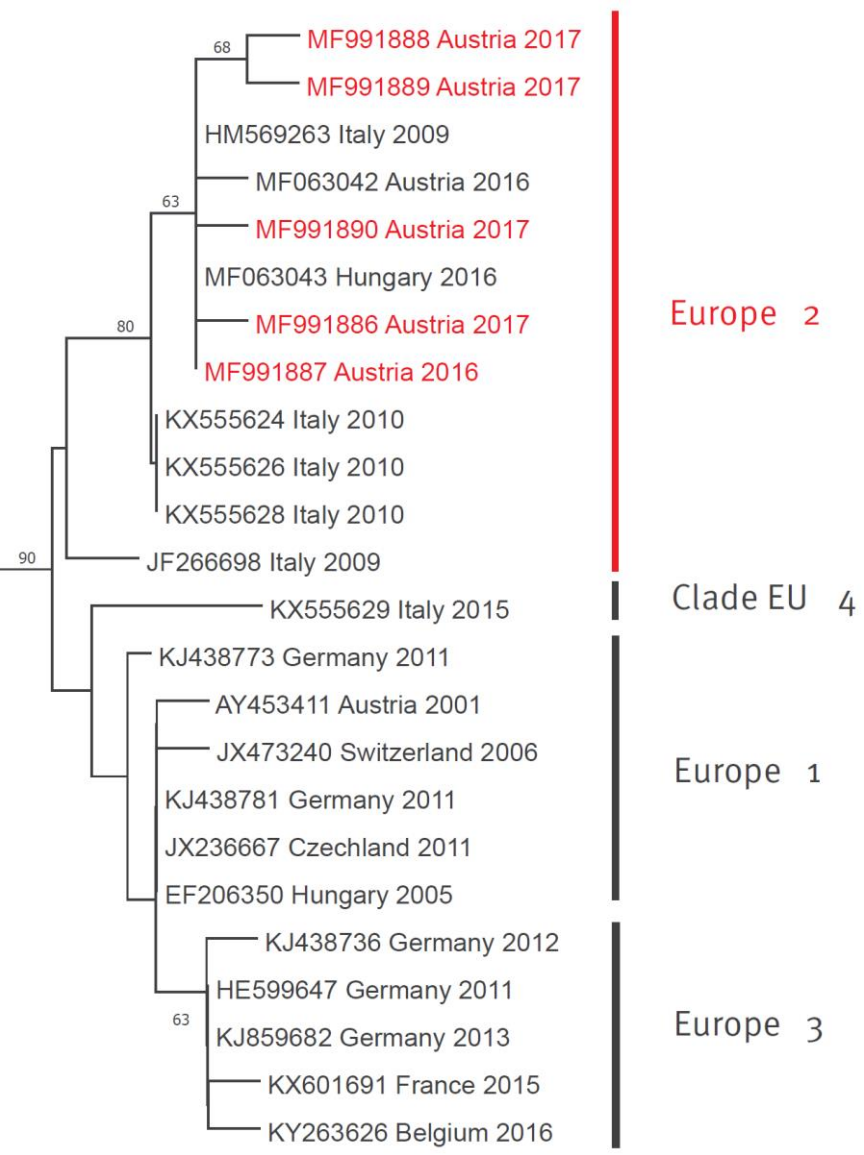
During summer 2016, one of 12,047 blood donations from western Germany, was tested positive for Usutu virus RNA.



Year	Number of plasma samples	Usutu virus RNA positive
2012	4200	0
2015	12,456	0
2016	12,047	1 (0.008 %)
2017	16,230	0

follow up sample (2 months later)		
Virus	IgM titer (IFA)	IgG titer (IFA)
Usutu	1:640	1:1,280
West Nile	1:160	1:160
Japan. Enc.	1:80	1:640

During summer 2017, six of 12,047 blood donations from eastern Austria, were tested positive for Usutu virus RNA.



Year	Number of plasma samples	Usutu virus RNA positive
2015	74, 677	0
2016	70,864	1 (0.001 %)
2017	12,047	6 (0.05 %)

The surveillance study from the municipality of Modena (Italy) demonstrated that Usutu virus infection is not a sporadic event in humans and more frequent than West Nile virus infections.

Sample type	Number of samples	Usutu virus RNA positive	West Nile virus RNA positive
CSF	306	8 (2.6 %)	0
Sera	609	2 (0.3 %)	0

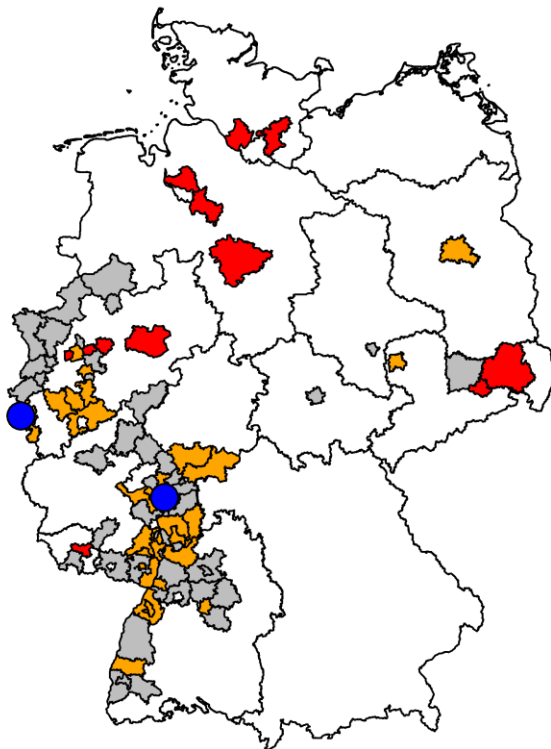
Year	Number of serum samples	Usutu virus nAb positive	West Nile virus nAb positive
2008	244	14 (5.7 %)	5 (2.1 %)
2009	306	21 (6.9 %)	11 (3.6 %)
2010	45	4 (8.9 %)	1 (2.2 %)
2011	14	1 (7.1 %)	1 (7.1%)

Increased vigilance for acute human Usutu virus infections since the beginning of the epizootic in western Europe

Country	Year	Number of cases	Clinical presentation	Comorbidities
Central African Republic	1981	1	fever and rash	-
Burkina Faso	2004	1	fever and jaundice	-
Italy	2008 - 2009	15	meningoencephalitis / encephalitis	large B cell lymphoma, thrombotic thrombocytopenic purpura, liver disease, diabetes, hypertension, mitral insufficiency
Germany	2011	1	asymptomatic	none
Croatia	2013	3	meningoencephalitis	diabetes
Germany				none
			asymptomatic	none
France	2016	1	facial palsy	none

No case of transfusion-associated Usutu fever !

Outlook



- positive birds before '17
- positive birds before and in '17
- positive birds for the first time in '17
- human cases ('12, '16)

- **Usutu virus-specific molecular and serological assays**
- **Simple point-of-care diagnostics (Ag, Ab or RNA)**
- **Usutu virus EQAs**
- **Increased syndromic surveillance**
- **Targeted and sustainable vector control measures**
- **Vector competence studies**



Thank you for your attention !