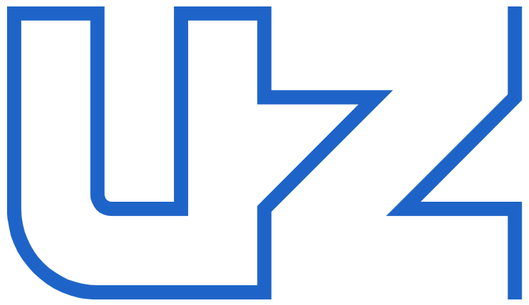

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Steven Callens / Dept. General Internal Medicine

Emergence of arbovirus related disease in Europe

The times, they are a’changing

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INTRODUCTION

01 Vector-borne diseases are infections transmitted by the bite of infected arthropod species, such as mosquitoes, ticks, triatomine bugs, sandflies, and blackflies.

02 Arthropod vectors are cold-blooded (ectothermic) and thus especially sensitive to climatic factors.

03 Weather influences survival and reproduction rates of vectors, in turn influencing habitat suitability, distribution and abundance; intensity and temporal pattern of vector activity (particularly biting rates) throughout the year; and rates of development, survival and reproduction of pathogens within vectors.

04 Vector-borne diseases account for 17% of worldwide infectious diseases

Ref http://ecdc.europa.eu/en/climate-change/climate-change-europe/vector-borne-diseases ;
Infection Ecology and Epidemiology 2015, 5: 28132 - http://dx.doi.org/10.3402/iee.v5.28132

KNOWN HUMAN PATHOGENIC ARBOVIRUS

Family Bunyaviridae

Genus Nairovirus

- Crimean–Congo hemorrhagic fevervirus (CCHF)

Genus Orthobunyavirus

- Bunyamwera virus
- California encephalitis virus
- Jamestown Canyon virus (JCV)
- La Crosse encephalitisvirus (LACV)

Genus Phlebovirus

- Rift Valley fever virus(RVFV)
- Toscana virus (TOSV)
- Heartland virus

Family Flaviviridae

Genus Flavivirus

- Tick-borne viruses
  - Mammalian tick-borne virus group
    - Kyasanur forest disease virus (KFDV)
    - Tick-borne encephalitis virus (TBEV)
- Mosquito-borne viruses
  - Dengue virus group
    - Dengue virus(DENV)
  - Japanese encephalitis virus group
    - Japanese encephalitisvirus (JEV)
    - Murray Valley encephalitis virus (MVEV)
    - St. Louis encephalitisvirus (SLEV)
    - West Nile virus(WNV)
  - Spondweni group
    - Spondweni virus
    - Zika virus(ZIKV)
  - Yellow fever virus group
    - Yellow fevervirus (YFV)

Family Reoviridae

Subfamily Sedoreovirinae

- Genus Orbivirus
  - African horse sickness virus(AHSV)
  - Bluetongue disease virus(BTV)
  - Equine encephalosis virus(EEV)
- Genus Seadornavirus
  - Banna virus (BAV)
- Subfamily Spinareovirinae
  - Genus Coltivirus
    - Colorado tick fevervirus (CTFV)

Family Togaviridae

Family Togaviridae

- Genus Alphavirus
  - Eastern equine encephalitis virus(EEE)
  - Ross River virus(RRV)
  - Venezuelan equine encephalitis virus(VEE)
  - Western equine encephalitis virus(WEE)
  - Chikungunya virus(CHIKV)

EUROPE: VULNERABLE TO VECTOR BORNE DISEASES

Increased globalization, landscape management and changing socio economic behavior create suitable conditions for the (re)emergence of vector-borne diseases in Europe

- Increased tourism
- Increased worldwide trade
- Economic variables
- Demographic variables

Risks associated with vectors

- The import of an exotic species that can transmit an arbovirus,
- The import of an arbovirus that is transmitted by an exotic established mosquito,
- The import of an arbovirus that is transmitted by indigenous species.

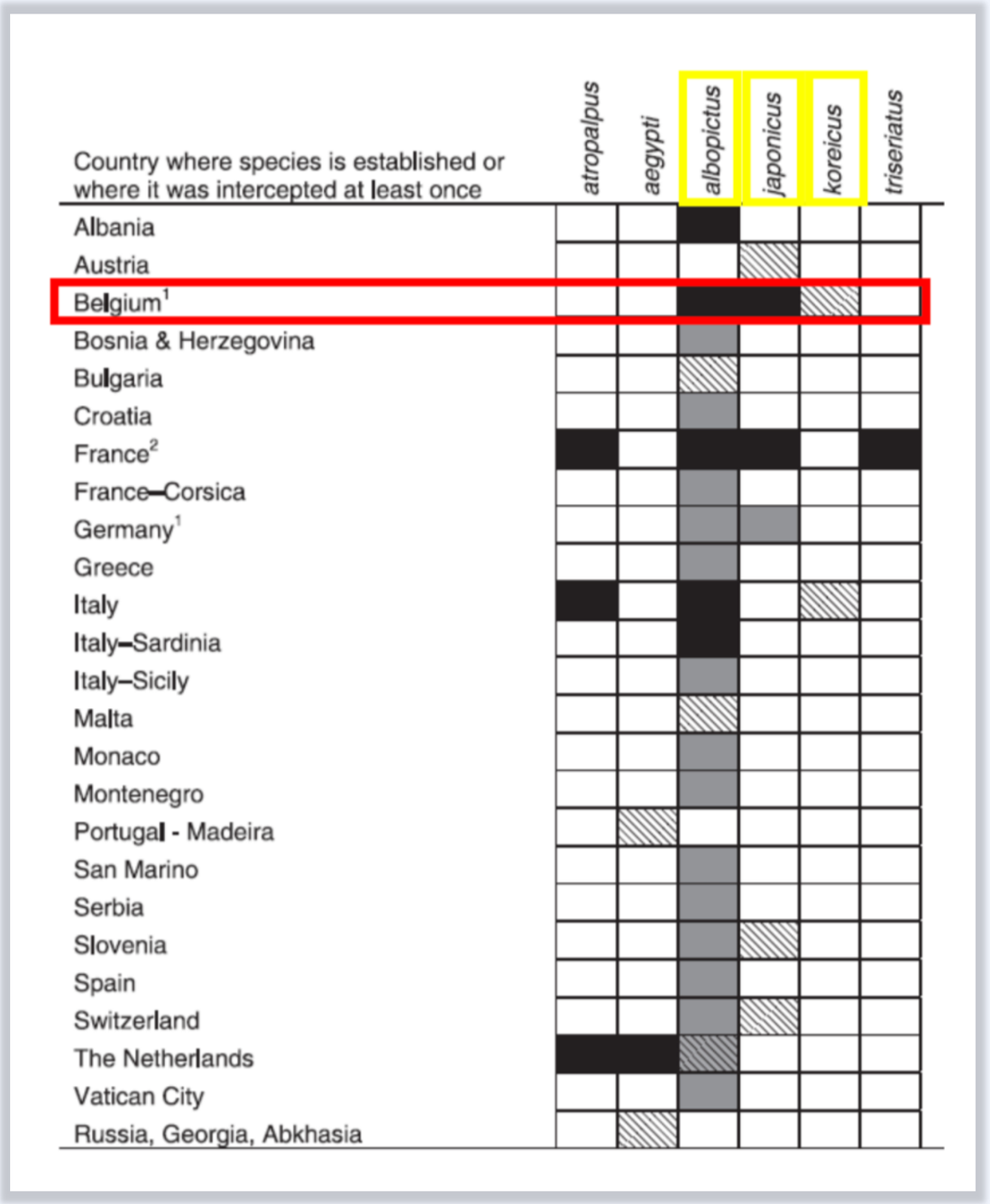
IMPORTATION ROUTES OF THE EXOTIC AEDINE MOSQUITOES ESTABLISHED OR INTERCEPTED IN EUROPE

Used tire trade
Both used tire and Lucky bamboo trades
Public/private ground transport
Unknown route of import
Species not present

[1] *Aedes albopictus* was not able to establish in Belgium or Germany.

[2] *Ae. albopictus* established successfully via ground transport.

DOI: 10.1089/vbz.2011.0814



Country where species is established or where it was intercepted at least once	*atropalpus*	*aegypti*	*albopictus*	*japonicus*	*koreicus*	*triseriatus*
Albania			■			
Austria				▨		
Belgium[1]			■	■	▨	
Bosnia & Herzegovina			▒			
Bulgaria			▨			
Croatia			▒			
France[2]	■		■	■		■
France–Corsica			▒			
Germany[1]			▒	▒		
Greece			▒			
Italy	■		■		▨	
Italy–Sardinia			■			
Italy–Sicily			▒			
Malta			▨			
Monaco			▒			
Montenegro			▒			
Portugal - Madeira		▨				
San Marino			▒			
Serbia			▒			
Slovenia			▒	▨		
Spain			▒			
Switzerland			▒	▨		
The Netherlands	■	■	▨			
Vatican City			▒			
Russia, Georgia, Abkhasia		▨				

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MOSQUITO BORN DISEASES - WEST NILE FEVER

Family:

Flaviviridae which is part of the Japanese encephalitis antigenic group

Infects birds and infrequently humans

Vector:

Culex mosquito

- In epidemic in France (2000) **aggressiveness of the vector** (*Culex modestus*) **was positively correlated with temperature and humidity**, and linked to rainfall and sunshine
- Epidemic in Romania linked to high minimum temperature (during summer heat wave)
  - Optimal conditions is higher than normal minimum temperature (heat wave during summer) following mild winter and dry spring
  - **Dry spells favor reproduction of city dwelling vectors** (*Culex pipiens*) as vectors and host are concentrated round water sources, leading to arbovirus multiplication

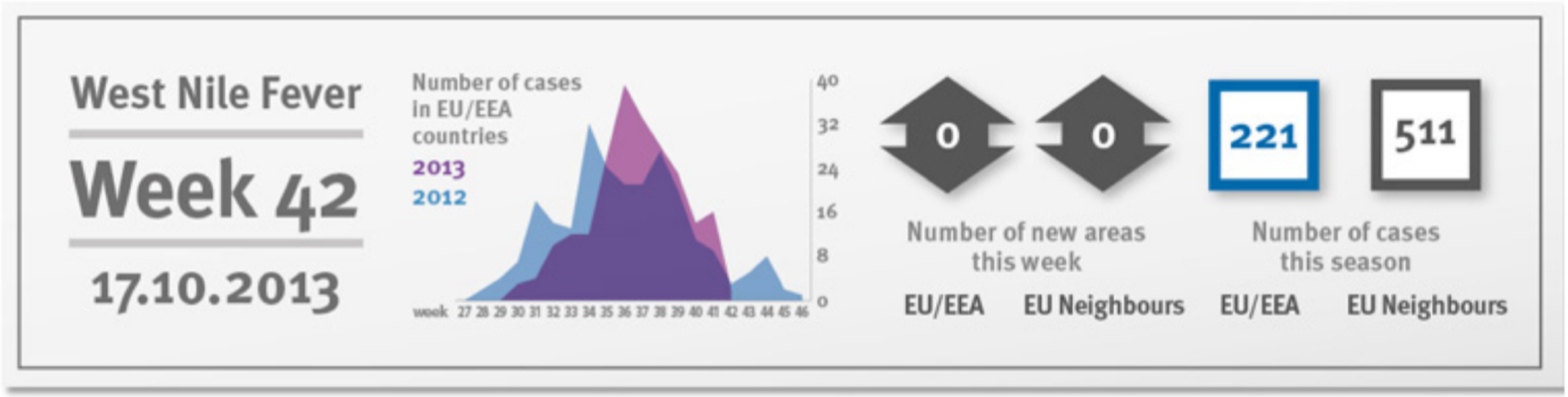
Ref: http://ecdc.europa.eu/en/climate-change/climate-change-europe/vector-borne-diseases

WEST NILE VIRUS IN A BELGIAN TRAVELER

A 73-year-old Belgian woman, who had a medical history of lymphoma, traveled to Kavala city (Macedonia, Greece)

Developed 6-day history of fever, headache, malaise, nausea, confusion, decline of consciousness, and neck stiffness.

Latest human cases reported from Italy, Montenegro. Spain reported cases in horses



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MOSQUITO BORN DISEASES - DENGUE

Family:
Flaviviridae

Vector:
Aedes aegypti
(yellow fever mosquito)

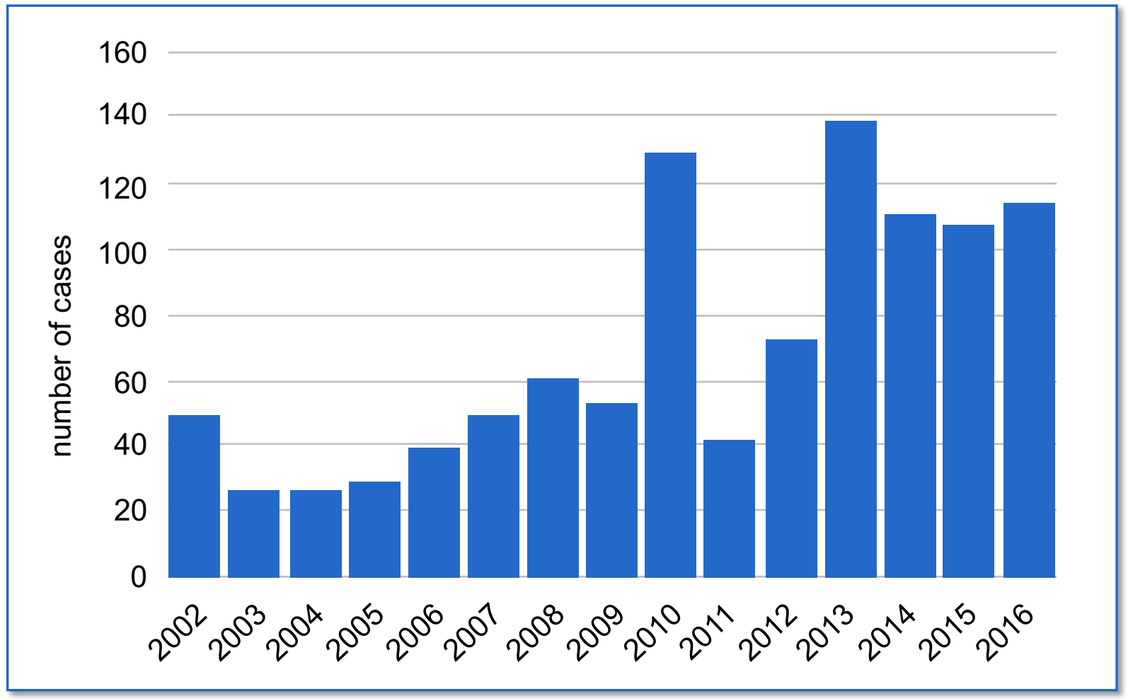
Over the last 15 years another competent vector Aedes albopictus (Asian tiger mosquito) has been introduced into Europe and expanded into several countries, raising the possibility of dengue transmission.

With increased temperature

- Shift of transmission broader latitudinal and altitudinal range
- Increased transmission season

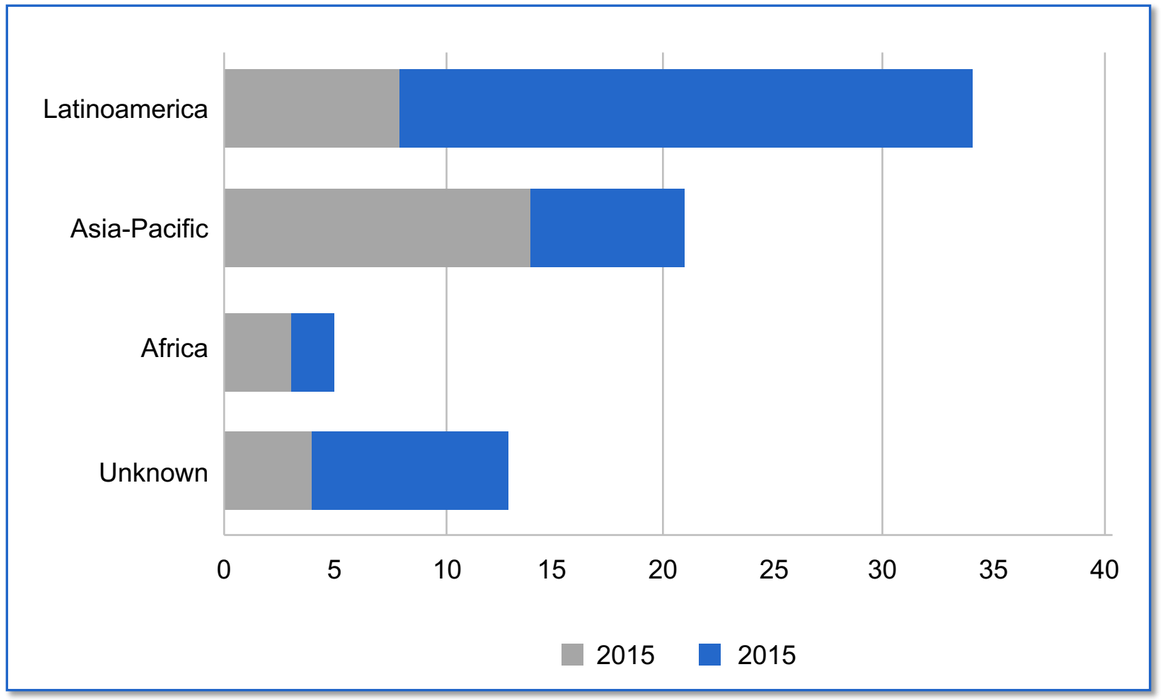
Ref http://ecdc.europa.eu/en/climate-change/climate-change-europe/vector-borne-diseases

DENGUE EPIDEMIOLOGY IN BELGIUM



Figuur 1: **Aantal Dengue gevallen gerapporteerd per jaar, België, 2006-2016**

(Bron: referentielaboratorium/NRC voor Dengue)



Figuur 2: **Aantal Dengue gevallen gerapporteerd per plaats van besmetting, België, 2015-2016**

(Bron: referentielaboratorium/NRC voor Dengue)

MOSQUITO BORN DISEASES - CHIKUNGUNYA

Family:
Togaviridae

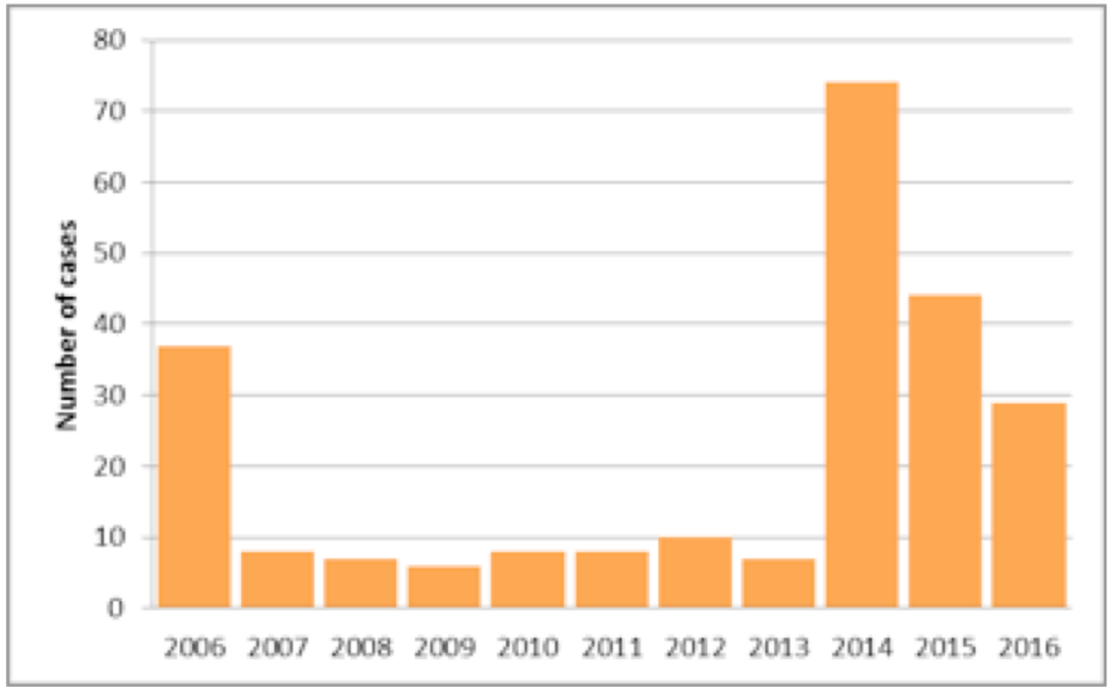
Vector:
Aedes albopictus

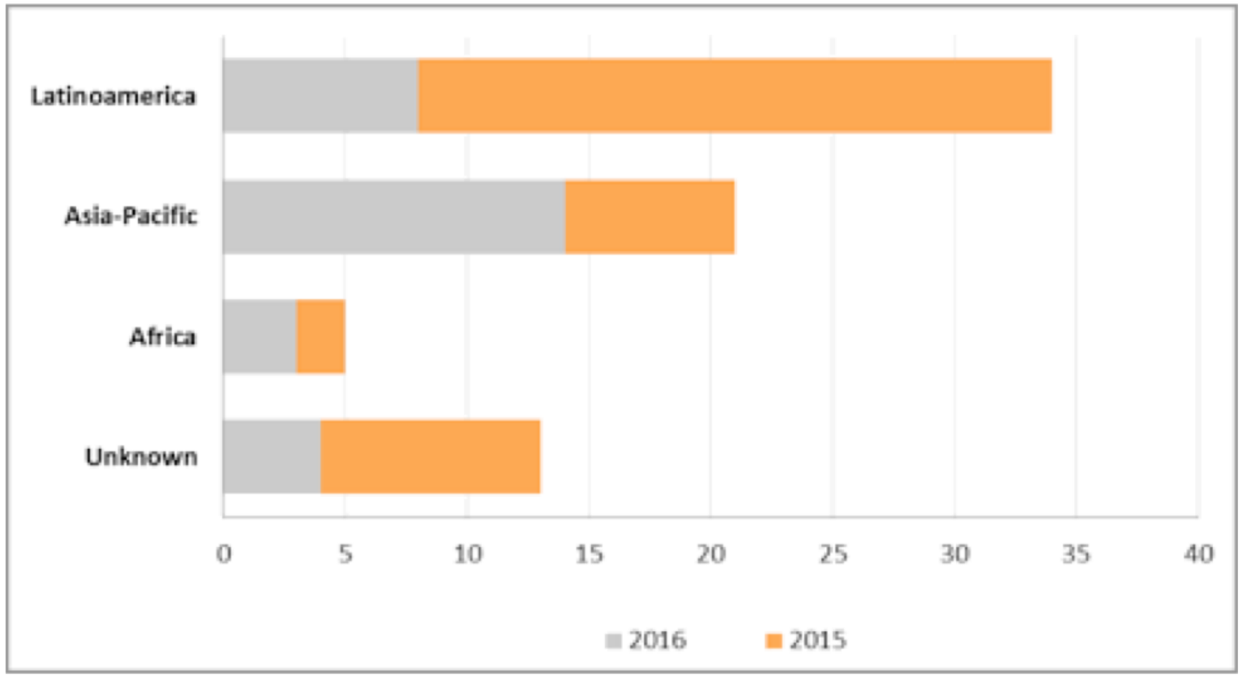
First confirmed outbreak
2007 Italy

Models suggest vector dependency on **mild winters**, mean annual **rainfall** exceeding 50 cm and mean summer temperatures exceeding 20°C, in addition to **duration of seasonal activity** (time between egg hatching and autumn egg diapose)

Ref http://ecdc.europa.eu/en/climate-change/climate-change-europe/vector-borne-diseases

CHIKUNGUNYA EPIDEMIOLOGY IN BELGIUM





Figuur 1: **Aantal Chikungunya gevallen gerapporteerd per jaar, België, 2006-2016**

(Bron: referentielaboratorium/NRC voor Dengue)

Figuur 2: **Aantal Chikungunya gevallen gerapporteerd per plaats van besmetting, België, 2015-2016**

(Bron: referentielaboratorium/NRC voor Dengue)

FIRST CASES OF AUTOCHTHONOUS DENGUE FEVER AND CHIKUNGUNYA FEVER IN FRANCE:

FROM BAD DREAM TO REALITY

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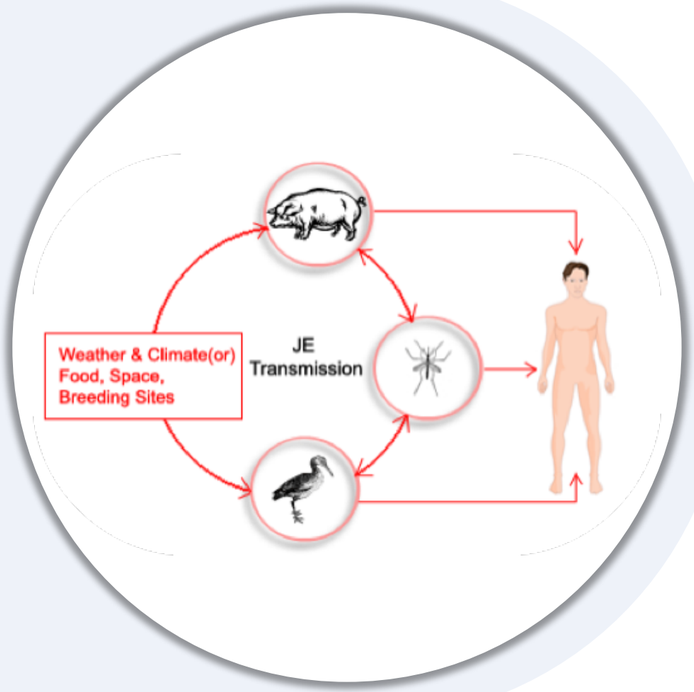
JAPANESE ENCEPHALITIS (IN EUROPE)



Italy: JEV NS5 gene (expected size, 215 bp) were obtained from tissues of six birds collected in 2000

Limited JEV circulation has occurred between birds and mosquitoes in Italy but no human cases have been observed, as in Australia since 1995.

- Relatively low availability of amplifying hosts (pigs) in that area
- Low vector competence of European *Culex pipiens*
- Low capability of local birds to maintain a persistent JEV circulation or other factors suppressing the JEV epidemic cycle, and
- Limited or absent human exposure.

Laboratory differential diagnosis of neuroinvasive cases occurring in humans and horses during the mosquito season may have to include JEV in the panel of viruses

Euro Surveill. 2012;17(32):pii=20241 -
Euro Surveill. 2012;17(32):pii=20242

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LITTLE KNOWN HUMAN PATHOGENIC ARBOVIRUS

VOGELBESCHERMING ROEPT OP OM ZIEKE VOGELS TE MELDEN

Usutu-virus houdt lelijk huis onder merels van Merelbeke

Het Afrikaanse usutu-virus is opgedoken in het Gentse en houdt lelijk huis in de lokale merelpopulatie. Bij het opvangcentrum in Merelbeke komen elke dag zieke vogels binnen.

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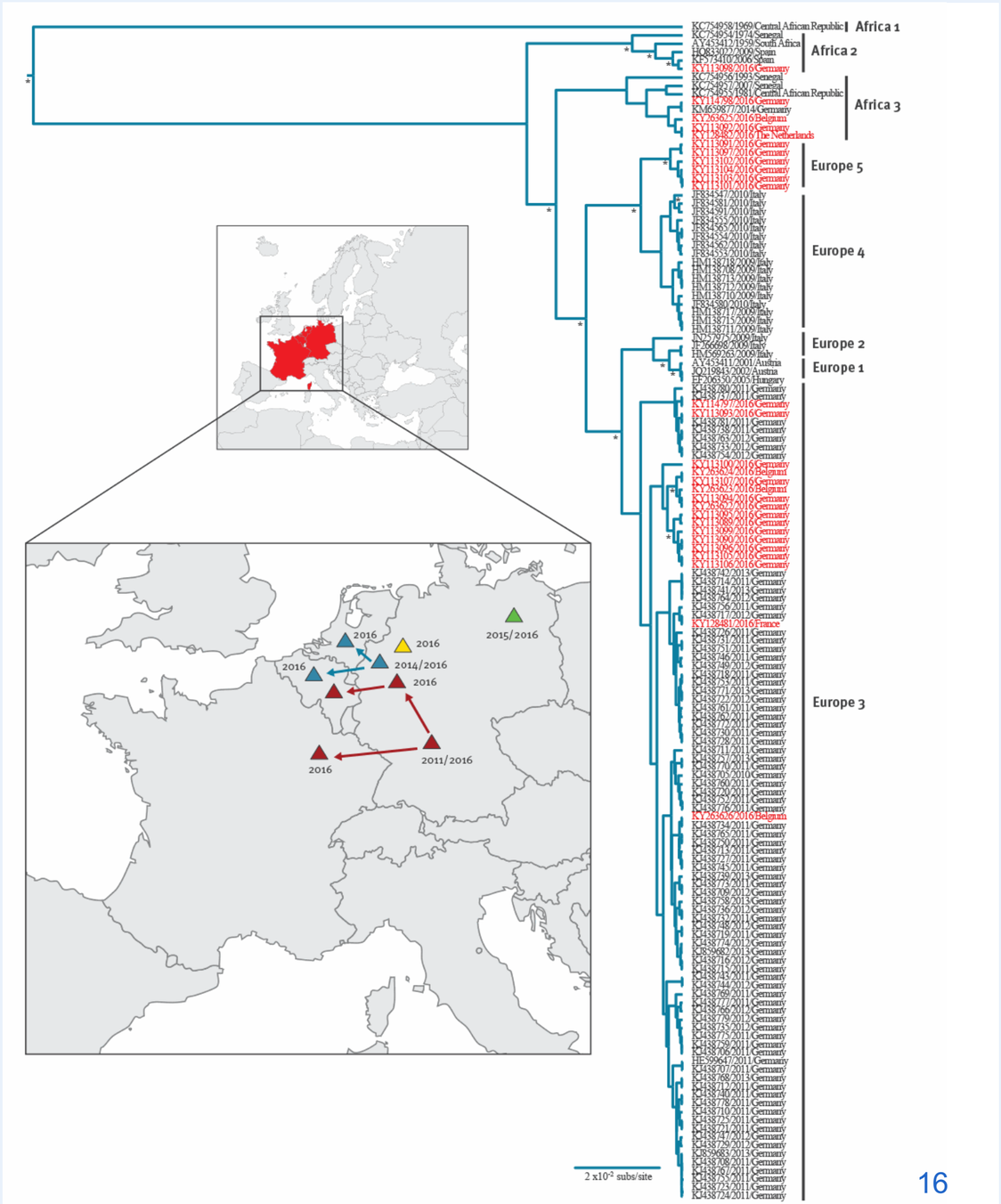
USUTU VIRUS

Of the 17 live and 147 dead USUV-positive birds reported in 2016, 120 were detected in the tristate area of Belgium, Germany and the Netherlands. The spatial distribution of the majority of positive cases in 2016fell in an area with a mean basic reproduction number larger than one (R0>1)

Since the first large outbreaks in the 2000s, USUV has become a potential public health concern given the increasing number of reported human infections

It can be speculated that the USUV lineages detected in Belgium, France and the Netherlands were most likely imported from Germany via infected semi-resident wild birds

The presence of a Europe 3 lineage strain in France and an Africa 3 strain in the Netherlands could each represent a single introduction event with Germany as possible source.



*Ref Cadar D, Lühken R, van der Jeugd H, et al. Widespread activity of multiple lineages of Usutu virus, Western Europe, 2016. Eurosurveillance 2017; **22**: 1–7.*

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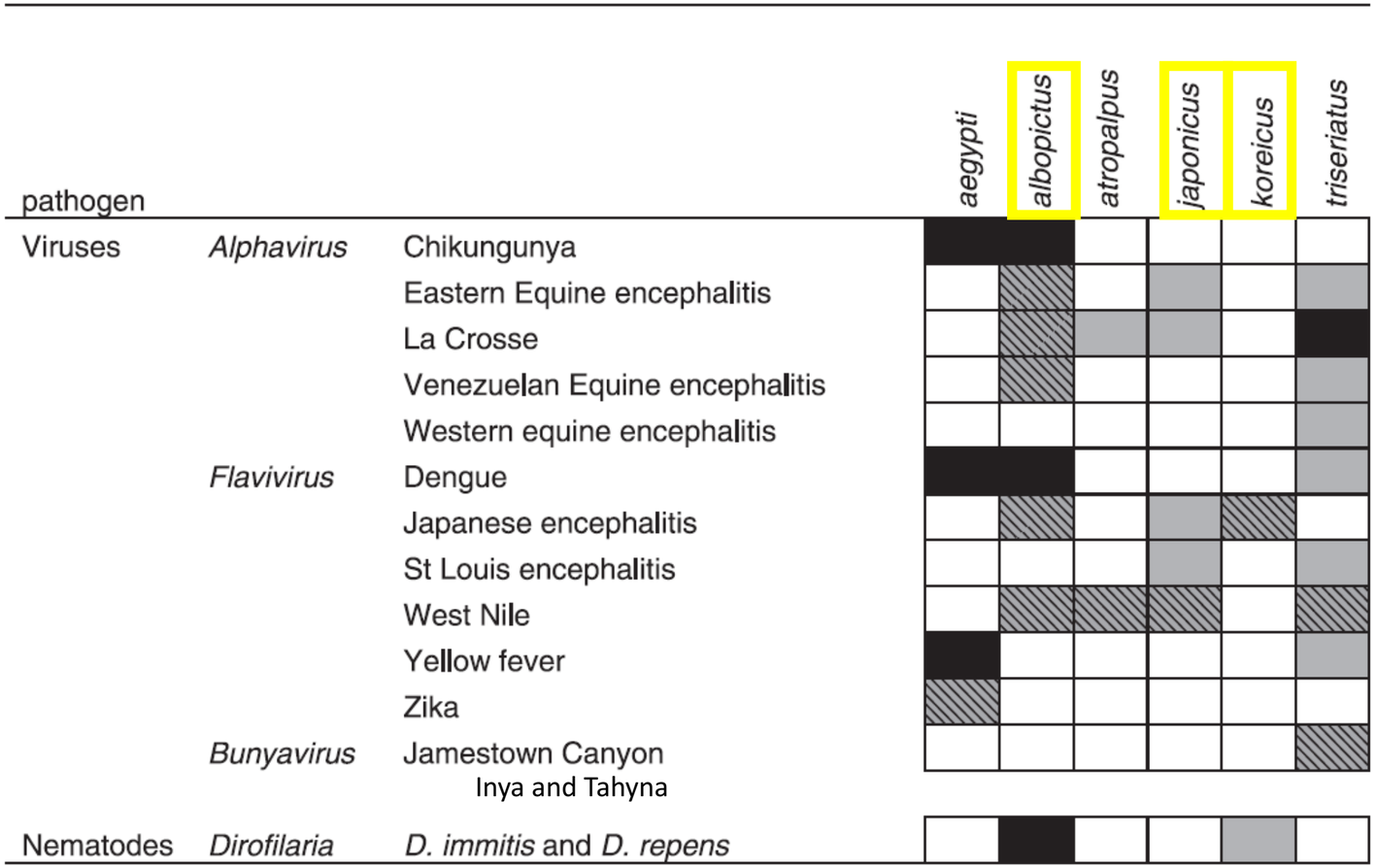
WHICH VECTORS ARE A THREAT?

Overview of the Vector Status of The Exotic Aedine Mosquito Species Intercepted or Established in Europe



Inya and Tahyna

Proven vector in the field

Found infected in field and laboratory. Competence studies having potential role as vector, but no proven vector in the field

Only laboratory. Competence studies having showed potential involvement in transmission

No vector or not known

DOI: 10.1089/vbz.2011.0814

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TICK-BORNE DISEASES -
TICK BORNE ENCEPHALITIS (TBE)

Family:
Flaviviridae

Vector (and reservoir):
predominantly *Ixodes ricinus*

Models:

Sweden: between 1960–98 increase in TBE incidence since the mid-1980s is related to **milder and shorter winters**, resulting in longer tick-activity seasons. In Sweden, the distribution-limit shifted to higher latitude ; the distribution has also shifted in Norway and Germany

Warmer and drier summers are part of the problem, *but also:*

- Changing land use patterns
- Increased density of large hosts for adults ticks (e.g. deer)
- Habitat expansion for rodent hosts
- Changes in alterations in recreational and occupational human activity (habitat encroachment), tourism
- Public awareness
- Vaccination coverage

Ref http://ecdc.europa.eu/en/climate-change/climate-change-europe/vector-borne-diseases

TICK BORN ENCEPHALITIS (SOURCE WIV/ISP)

In 2015 and 2016 one acute infection with TBEV was each time diagnosed in persons who had traveled and were not vaccinated. It was a 22-year-old man and a 44-year-old woman who were infected in Slovenia and Germany respectively.

The number of patients for whom a test was requested is increasing progressively and has doubled compared to the start of the NRC in 2012 (n = 44 versus 127 in 2016).

The increase in the number of requested tests in Belgium may indicate increased alertness for the disease.

- The strong increase in 2016 (especially in August and September) is probably linked to the establishment of the first autochthonous human infections in the Netherlands in the summer of 2016.
- Earlier that year, the exposure to TBEV in roe deer was demonstrated and the virus was also detected in ticks on the Sallandse Heuvelrug and the Utrechtse Heuvelrug.

Monitoring the risk of TBE in Belgium is best done on the basis of (serological) monitoring in animals.

- In 2014 and 2015, a total of 260 voles (Myodes glareolus, the main rodent reservoir of TBEV), and 47 forest mice (Apodemus sylvaticus) were captured by five researchers in the WIV-ISP in five locations in Wallonia: all negative results.
- In 2017, research will carried out on wild boar in Flanders.
- Research on ticks is not carried out for the time being because
  - Testing large numbers of ticks does not guarantee the detection of the virus, even in endemic areas
  - Prevalence of TBEV ticks does not seem to be directly related to the incidence of TBE in humans.

TICK-BORNE DISEASES - CRIMEAN-CONGO HEMORRHAGIC FEVER (CCHF)

Family:
The bunyaviridae family

Vector:
Hyalomma spp ticks

Host:
Domestic and wild animals.

The virus is the most widespread tick-borne arbovirus and is found in the Eastern Mediterranean where there have been a series of outbreaks in Bulgaria in 2002 and 2003, in Albania and in Kosovo in 2001

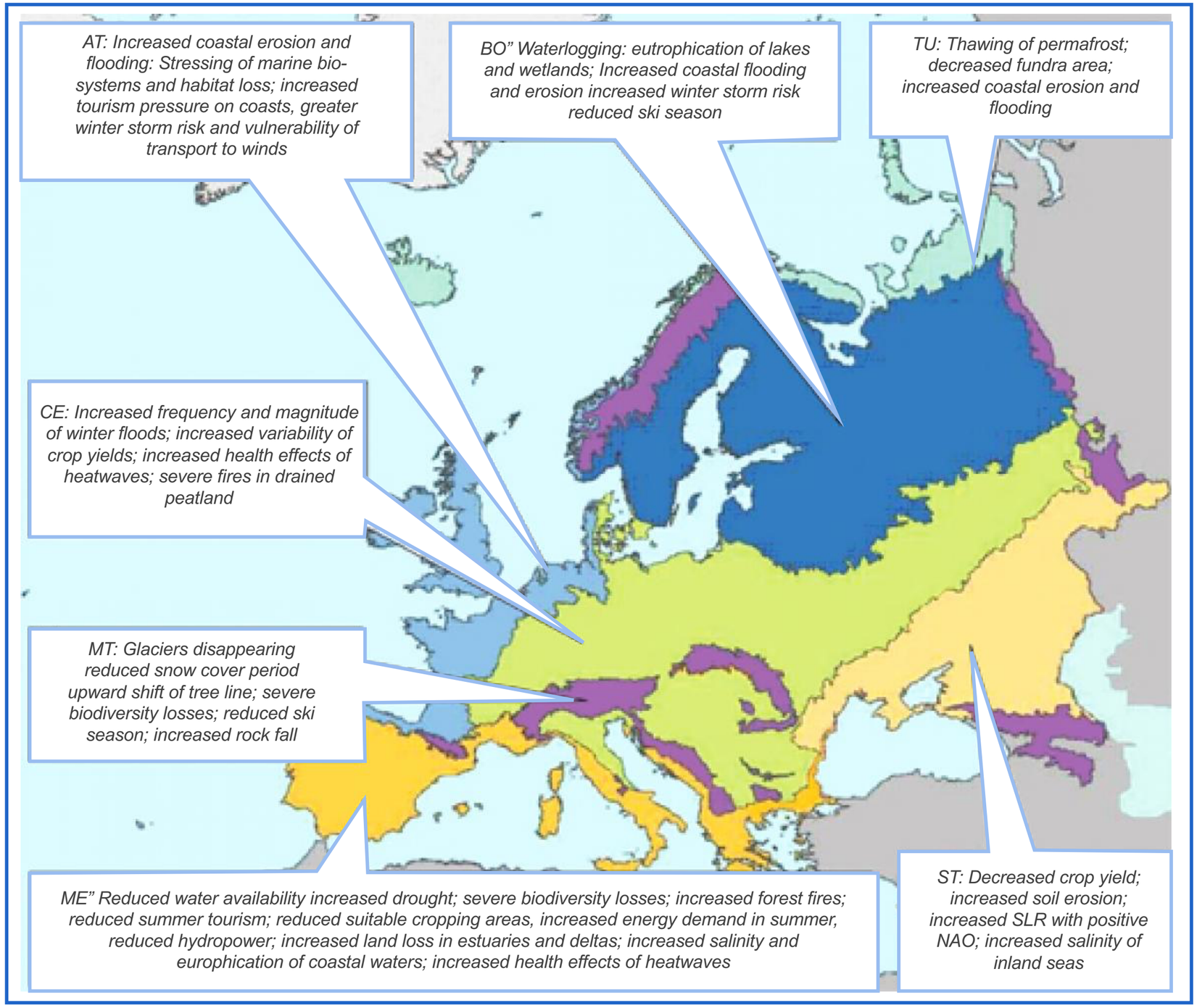
Models: Milder weather conditions, favouring tick reproduction may influence CCHF distribution

For example, an outbreak in Turkey was linked to a milder spring season (a substantial number of days in April with a mean temperature higher than 5°C) in the year before the outbreak. However, other factors such as land use and demographic changes have also been implicated.

Ref http://ecdc.europa.eu/en/climate-change/climate-change-europe/vector-borne-diseases

DRIVERS OF EMERGENCE OF ARBOVIRUS & OTHER VECTOR BORN DISEASES

Ref: Semenza JC, Menne B. Climate Change and Infectious Diseases in Europe. Lancet ID. 2009;9:365-75.



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DRIVERS OF EMERGENCE OF ARBOVIRUS & OTHER VECTOR BORN DISEASES

Climate change may alter the distribution and transmission of communicable diseases principally through

01 Impacting disease pathogens directly;

02 Impacting the distribution of vectors which may carry diseases;

03 Impacting human behaviours leading to changing patterns of exposure to infectious diseases (e.g. increased time spent outdoors in woodlands where ticks live).

Ref http://ecdc.europa.eu/en/climate-change/climate-change-europe

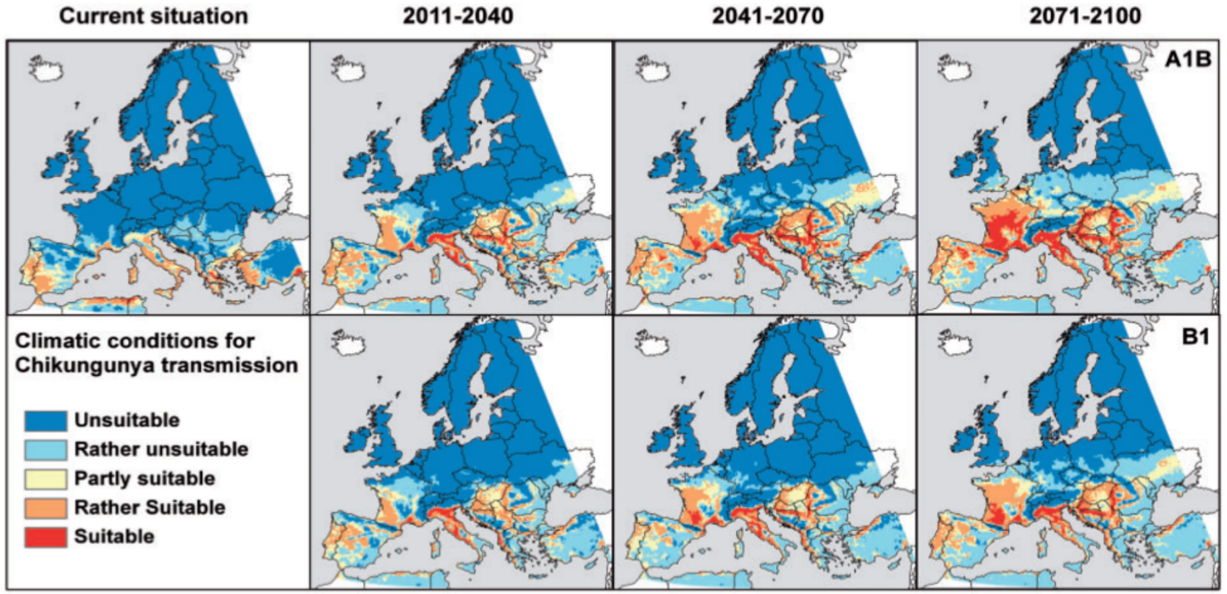

Figure Climatic risk map for chikungunya transmission in Europe generated by combining temperature requirements of the chikungunya virus with the climatic suitability of the vector Ae. albopictus.3 Projections for different time-frames are based on two emission scenarios (A1B and B1) from the Intergovernmental Panel on Climate Change, implemented in the regional climate model COSMO-CLM.

Ref: European Journal of Public Health, Vol. 24, No. 4, 531–532

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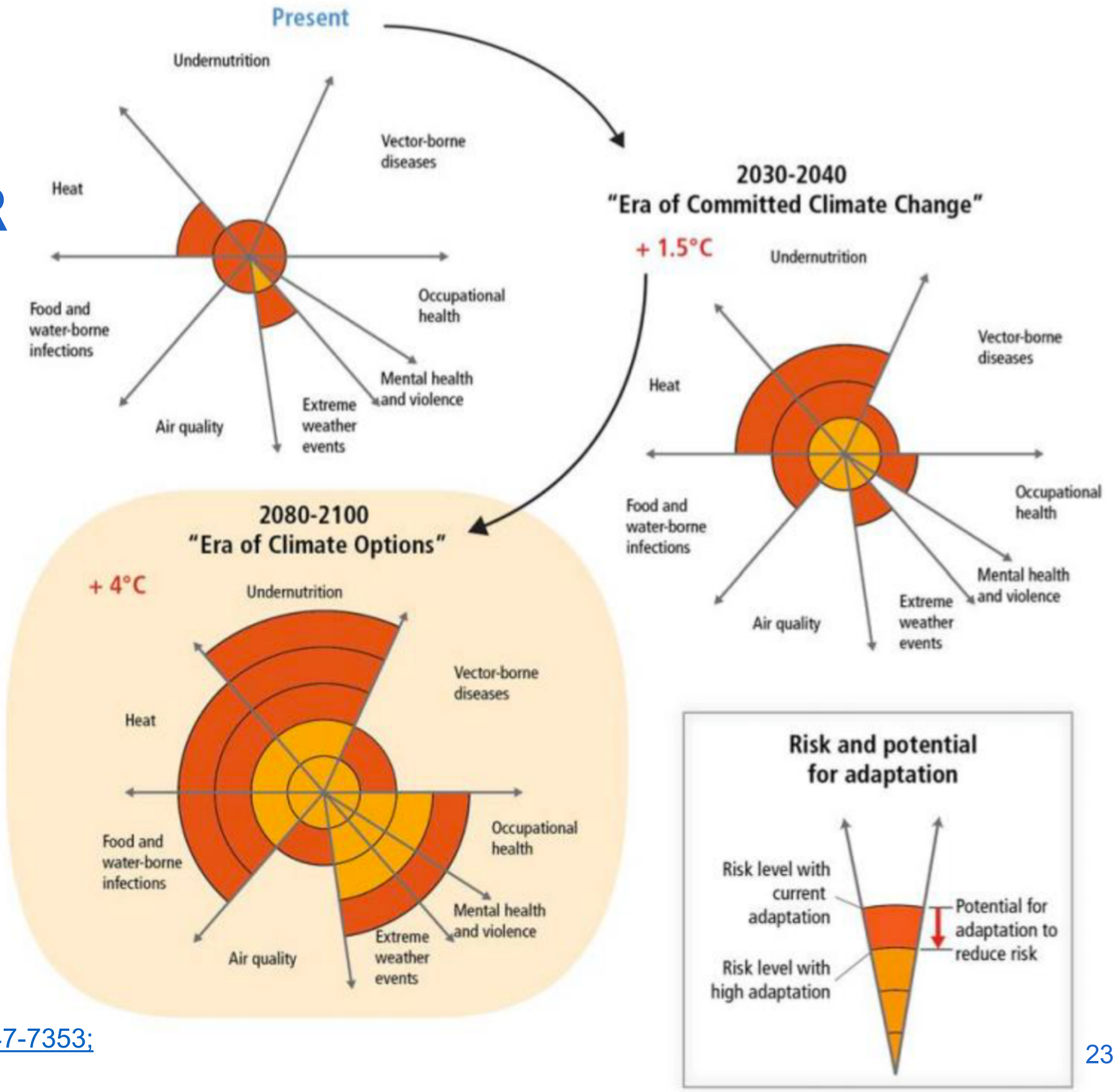
DRIVERS OF EMERGENCE OF ARBOVIRUS & OTHER VECTOR BORN DISEASES



But increased temperature and extreme weather conditions pose more problems than vector born diseases

Figure: ***Conceptual presentation of the health impacts from climate change and the potential for impact reduction through adaptation.***

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REF: Int. J. Environ. Res. Public Health 2014, 11, 7347-7353; doi:10.3390/ijerph110707347

FRAMING HEALTH MATTERS

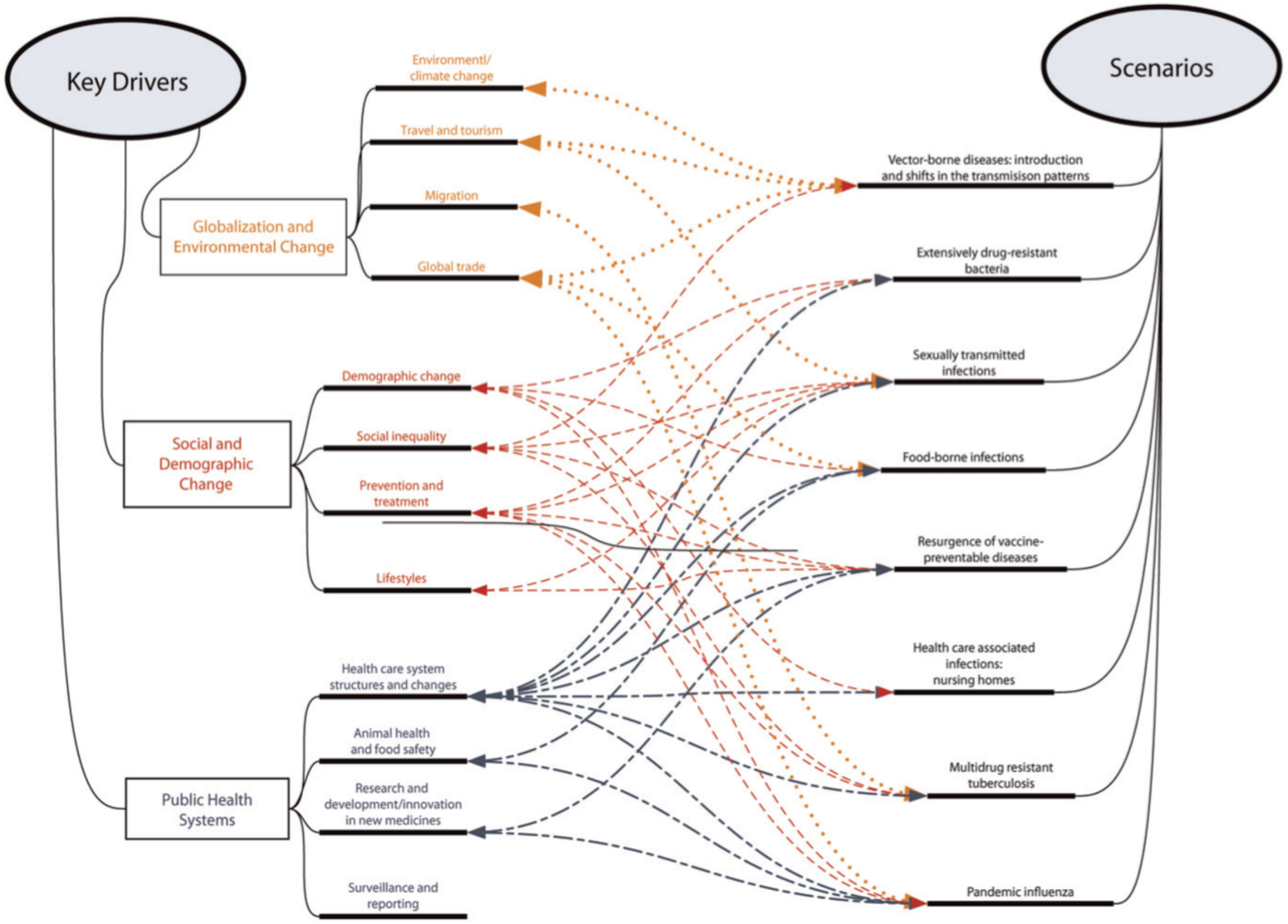
Human Behavior - Socio-economic factors

- Trade (e.g. importing cargo in coastal areas with higher temperature might establish a competent vector - *Aedes*)
- Travel
- Land use and land management
- Economic downturn
  - In the baltics, following the collapse of the Soviet union, rates of tick-borne encephalitis surged, due to
    - Increased unemployment
    - Lower vaccination coverage
    - Greater time spent harvesting and foraging food in the forests habited by ticks.
  - In US
    - 2007: Housing crisis led to abandoned houses and outdoor pools, which became infested with mosquitos larvae, increasing the transmission of West Nile virus

REF European Journal of Public Health, Vol. 24, No. 4, 531–532

Host behavior

- Migrating wildlife
- One health principle: especially birds



Note. Infectious disease drivers are grouped into 3 categories and connected to the 8 scenarios developed in the expert consultation. The connections shown reflect those used to develop the scenarios, but they are by no means a comprehensive network of possible interactions between drivers and disease scenarios.

FIGURE 1—Interactions between disease drivers and scenarios: European Union.

Ref American Journal of Public Health | November 2011, Vol 101, No. 11

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SURVEILLANCE

	Europe	Belgium
Disease	*Predict: european harmonised large scale patient-oriented pathogenesis research studies in response to severe id outbreaks –workpackage 7* *Multi-centre EuRopean study of MAjorInfectious Disease Syndromes*	NRC & Peillaboratoria
Vector	*Climate change in Europe* *Prototype Early Warning Systems for Vector-Borne Diseasesin Europe*	*ITG OP DE UITKIJK VOOR TIJGERMUGGEN*
Host	*Climate change in Europe*	
Climate	*Climate change in Europe*	

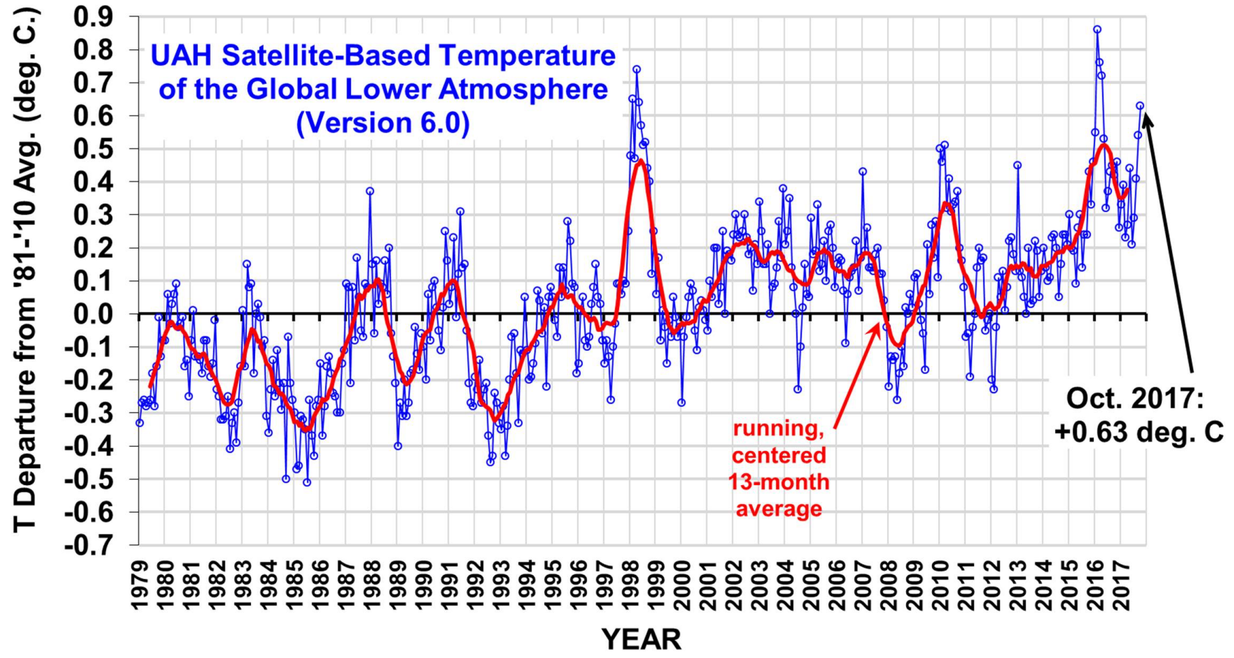
SURVEILLANCE (CONT)

Challenging for health care workers

- Think horse not zebra, but arbovirus is zebra
- Non specific symptoms
- No clinical consequence, in most cases, as treatment is supportive
- Microbiological detection method (serology, NAAT) are (were) restricted to few laboratories

Challenging for current surveillance

- Has only “recently” entered pubic health agenda
- Resources are dwindling, austerity limits vector & host surveillance



ONE HEALTH - HEALTH CARE IN A CONTINUUM

A paradigm shift to one health concept is necessary to win the global fight and prevent the emergence and spread of VBDs to new areas.

Failure is evident from West Nile Virus(WNV), Crimean-Congo hemorrhagic fever (CCHF), and Japanese encephalitis or CCHF, that has spread to more than 30 countries in a range of ecological conditions

Japanese encephalitis **unexpectedly emerged** in Australia, highly distant from the previous known outbreak in Indonesia;

The widespread establishment of WNV demonstrates the **vulnerability of non-endemic countries to the introduction of arboviruses**;

Wildlife is decimated by Usutu virus, yet little more than counting is done apparently

Economic damage due to bluetongue virus, and schmallenberg virus, transmitted by Culicoides biting midges, in ruminants in Europe, seems to portray a disturbing trend in the emergence of new disease threats associated with vector-borne pathogens that impact humans and livestock.

Ref Infection Ecology and Epidemiology 2015, 5: 28132 - http://dx.doi.org/10.3402/iee.v5.28132

ONE HEALTH –
(PUBLIC) HEALTH (CARE) IS JUST ONE SMALL FACTOR

The one health triad

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