# Transfusion-transmitted emerging infections - Current threats in Europe

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# Infectious threat to blood safety

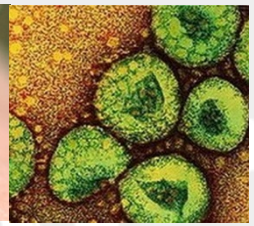
## Established infections

- HIV, HCV, HBV, CMV, HHV, HEV, malaria, Chagas disease, leishmaniasis…..
- PROVEN RISK - QUANTIFIABLE: PREVENTIVE MEASURES ESTABLISHED

## Emerging/re-emerging infections

- Unknown, unexpected and unrecognized
- THEORETICAL RISK – PRECAUTIONARY APP.
- PROVEN RISK – UNQUANTIFIABLE – PRECAUTIONARY APP.

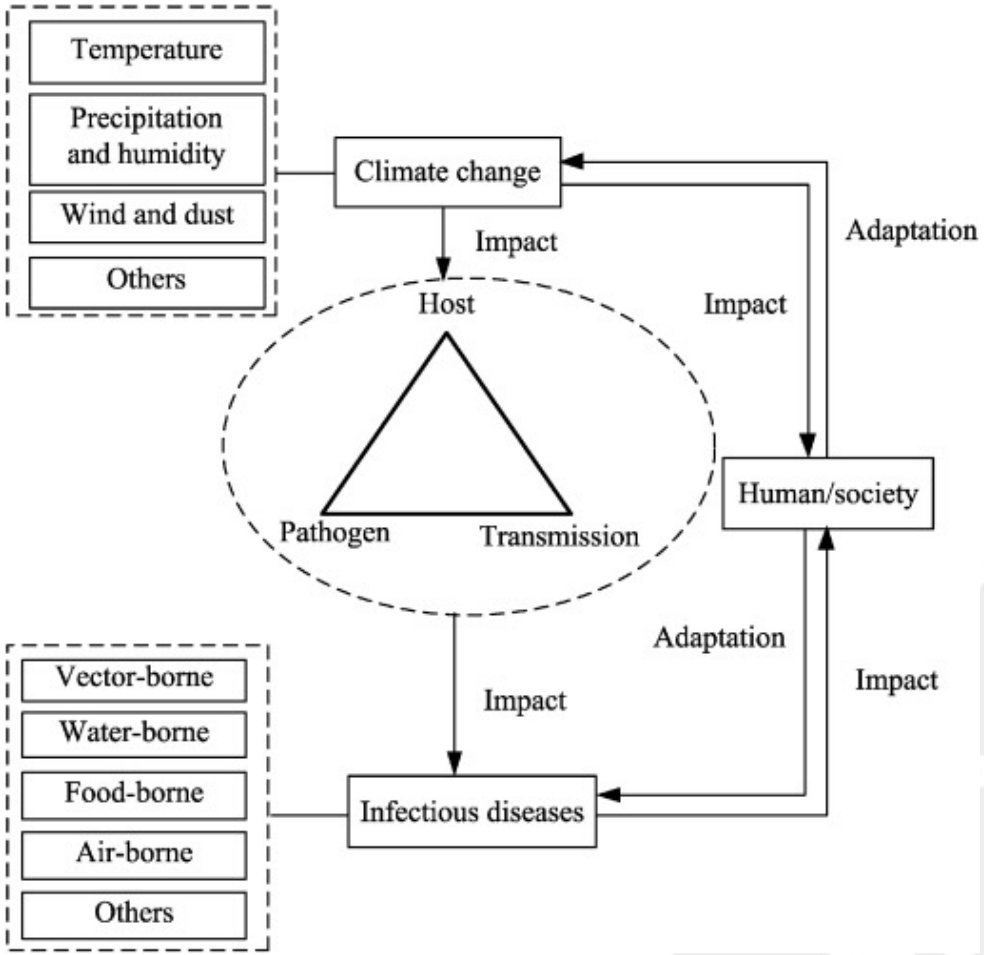


# MAJOR EID DRIVERS

- globalization and environmental change (including climate change, travel, migration, and global trade);
- social and demographic drivers (including population aging, social inequality, and life-styles);
- public health system drivers (including antimicrobial resistance, health care capacity, animal health, and food safety) and
- changes in the patterns of human behavior, social organization, urbanization, agriculture & animal husbandry

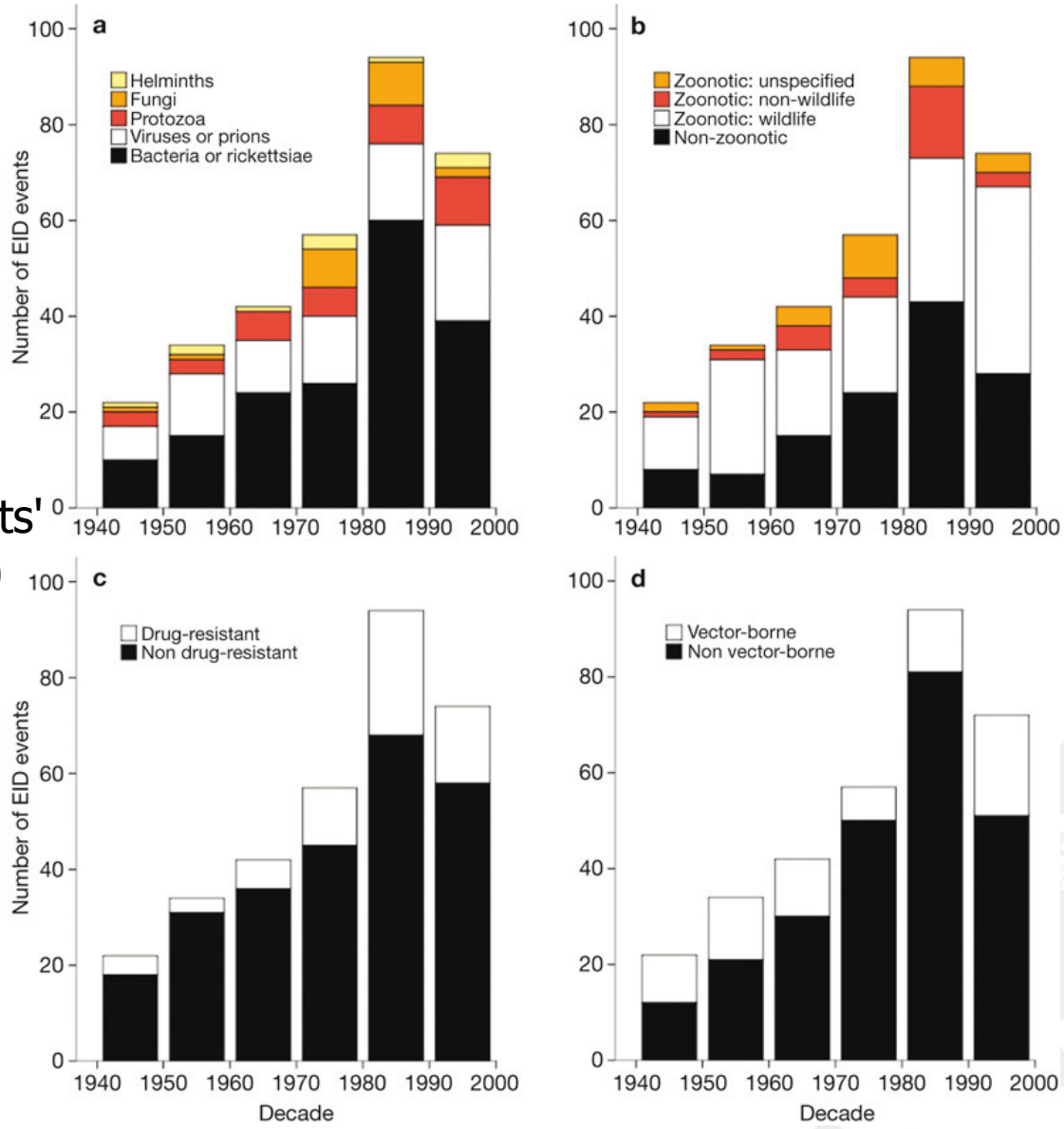
# Climate change, human infectious diseases, and humans/society.




Xiaoxu W et al. Impact of climate change on human infectious diseases: Empirical evidence and human adaptation. Environment International, Volume 86, 2016, 14–23.

# Trends in EIDS

335 EID 'events'
(1940 – 2004)




Jones KE et al. Global trends in emerging infectious diseases. Nature 451, 990-993, 2008.

# Climate change - possible mechanisms of acting on zoonotic and vector borne diseases

**Increased contacts of infected animal hosts and vectors with humans or with other hosts and vectors**

a) range shifts;

b) changes in the population density;

c) changes in the prevalence of pathogen in the host or vector population

**Increased likelihood that a human contact with host or vector would result in pathogen transmission**

a) changes in the pathogen load - changes in the rates of pathogen reproduction, replication, or development in hosts or vectors

Mills JN et al. Environ Health Perspect 118:1507–1514 (2010)

# Human population movements

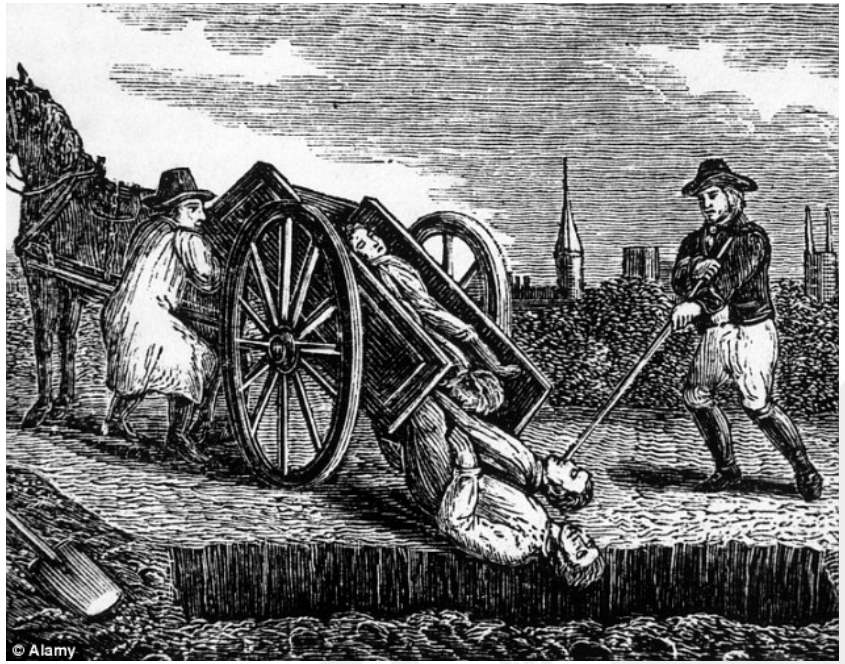
- Human movements are part of the dynamic global process of moving biota, along with plants, animals, microorganism and other materials
- Increased in numbers and speeds
- Diversity of destinations (remote areas-major population centres)
- Diversity of purpose (tourism, business, migration because of social, economic, or political upheavals or extreme events and environmental disasters)
- Humans can reach almost any part of the Earth today within the incubation period for most microbes that cause disease in humans
- Travel is also discontinuous, often including many stops and layovers along the way

# Consequences of the movements

- the juxtaposition of species that have never before had physical proximity (the contact between microbes, humans, and animals may result in infection)
- the establishment of species in new geographic areas (arthropods, mammals and other animals, and plants) may cause disease in immunologically naïve population or major changes in the existing ecosystem.

# Spread of plague during fourteenth century


# Plague during fourteenth century in Europe



# Current threats to EU/EEA

**Active threats**

- **Yellow fever – Brazil**
- **Avian influenza A (H7N9) – China**
- **Zika virus – worldwide**

**Other threats**

- **West Nile virus**
- **dengue**
- **malaria**
- **chickungunya**

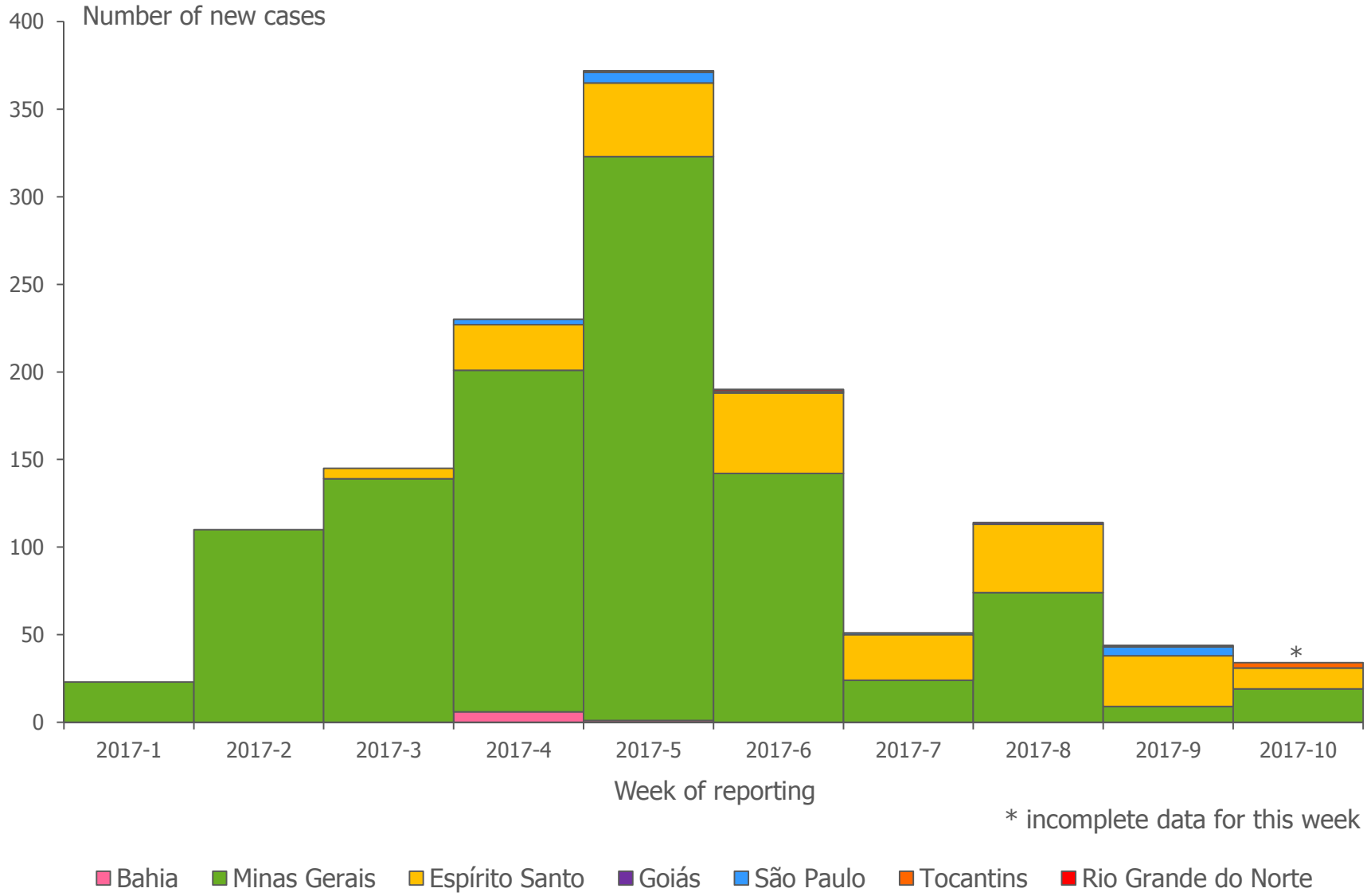
# Yellow fever - Brazil

6 January 2017, Brazil reported an outbreak of yellow fever. The index case had onset of symptoms on 18 December 2016.

As of 6 March 2017, Brazil has reported 1 337 cases (966 suspected and 371 confirmed),

During the past eight months,
four travel-associated cases of yellow fever were identified among EU travellers returning from South America.
one was returning from Suriname, two from Peru and one from Bolivia.
The significant increase  historical baseline (four cases between 1999 and July 2016).

**Distribution of suspected and confirmed human cases of yellow fever in Brazil from 1 January to 6 March 2017**



**Distribution of human cases of yellow fever in Brazil by state as of 6 March 2017**

| | All cases | Suspected cases | Confirmed cases |
|---|---|---|---|
| Minas Gerais | 1 057 | 769 | 288 |
| Espírito Santo | 226 | 147 | 79 |
| São Paulo | 15 | 11 | 4 |
| Bahia | 7 | 7 | 0 |
| Tocantins | 6 | 6 | 0 |
| Rio Grande do Norte | 1 | 1 | 0 |
| Goiás | 1 | 1 | 0 |
| Under investigation | 24 | 24 | 0 |
| **Total** | **1 337** | **966** | **371** |

**Distribution of confirmed human cases of locally-acquired yellow fever in Brazil, as of 7 March**


Confirmed cases of locally-acquired yellow fever, as of 07 March 2017

Municipalities with confirmed locally-acquired cases since 6 January 2017

Area at risk for yellow fever transmission

Area considered at no risk for yellow fever transmission

Federal state ★ *State capital city*

ECDC. Map produced on: 09 Mar 2017
ECDC map maker: https://emma.ecdc.europa.eu

# Yellow fever virus

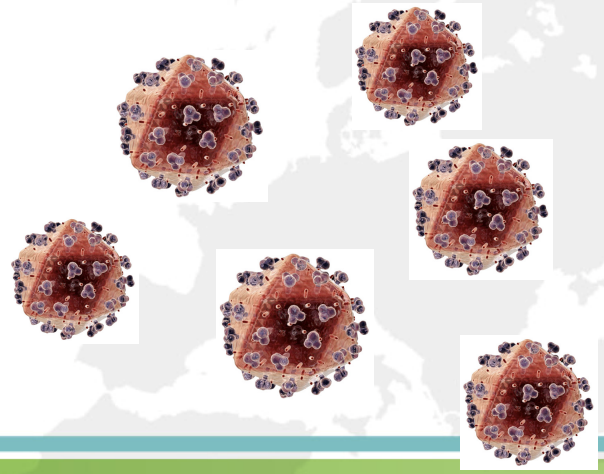
Type: Enveloped RNA virus

Family Flaviviridae

Genus: Flavivirus

Origin: East or Central Africa > West Africa > Europe > Americas (through slave trade)

Vector: Mosquitoes – AEDES species

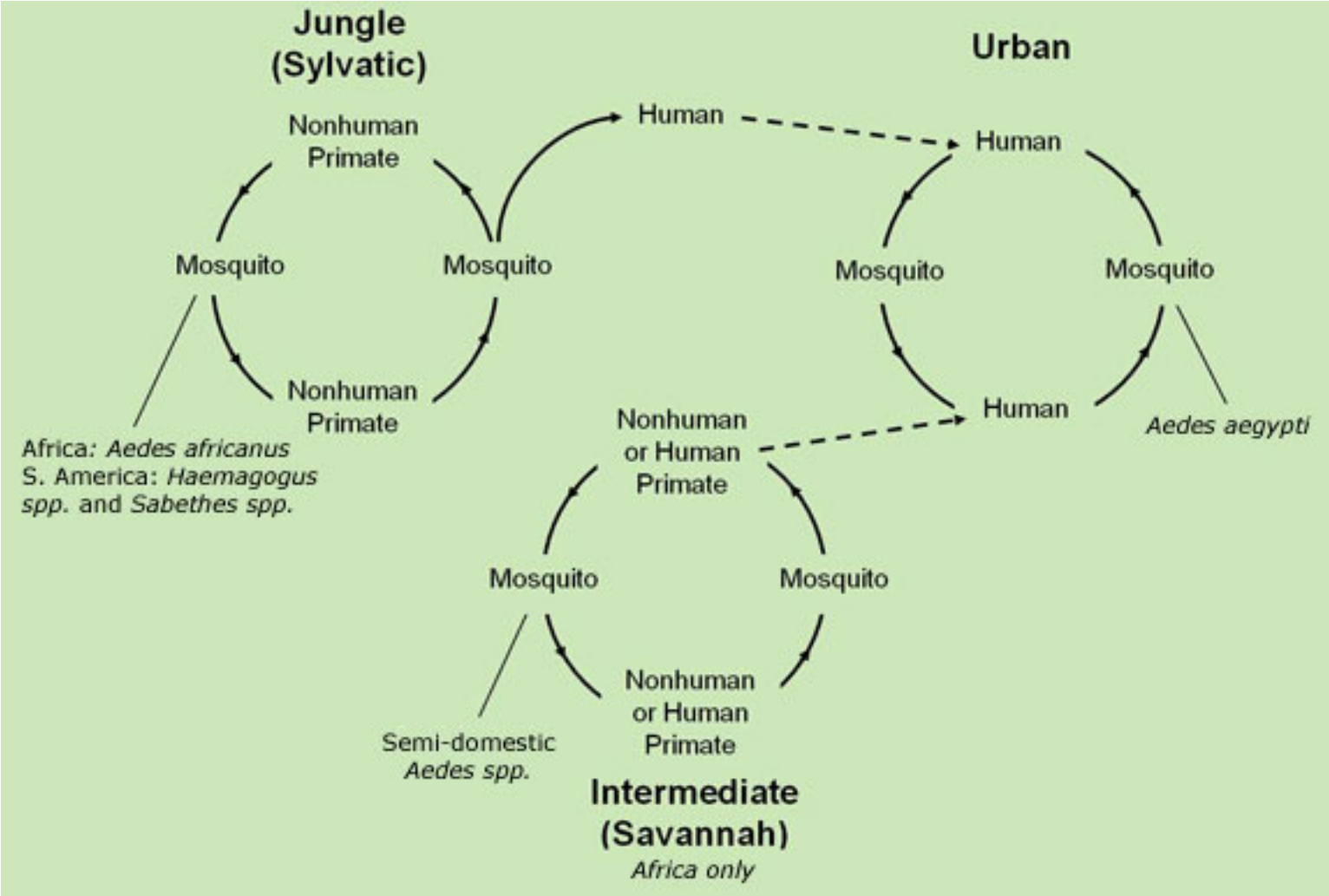


# Areas in Africa and South America where yellow fever is endemic, 2005

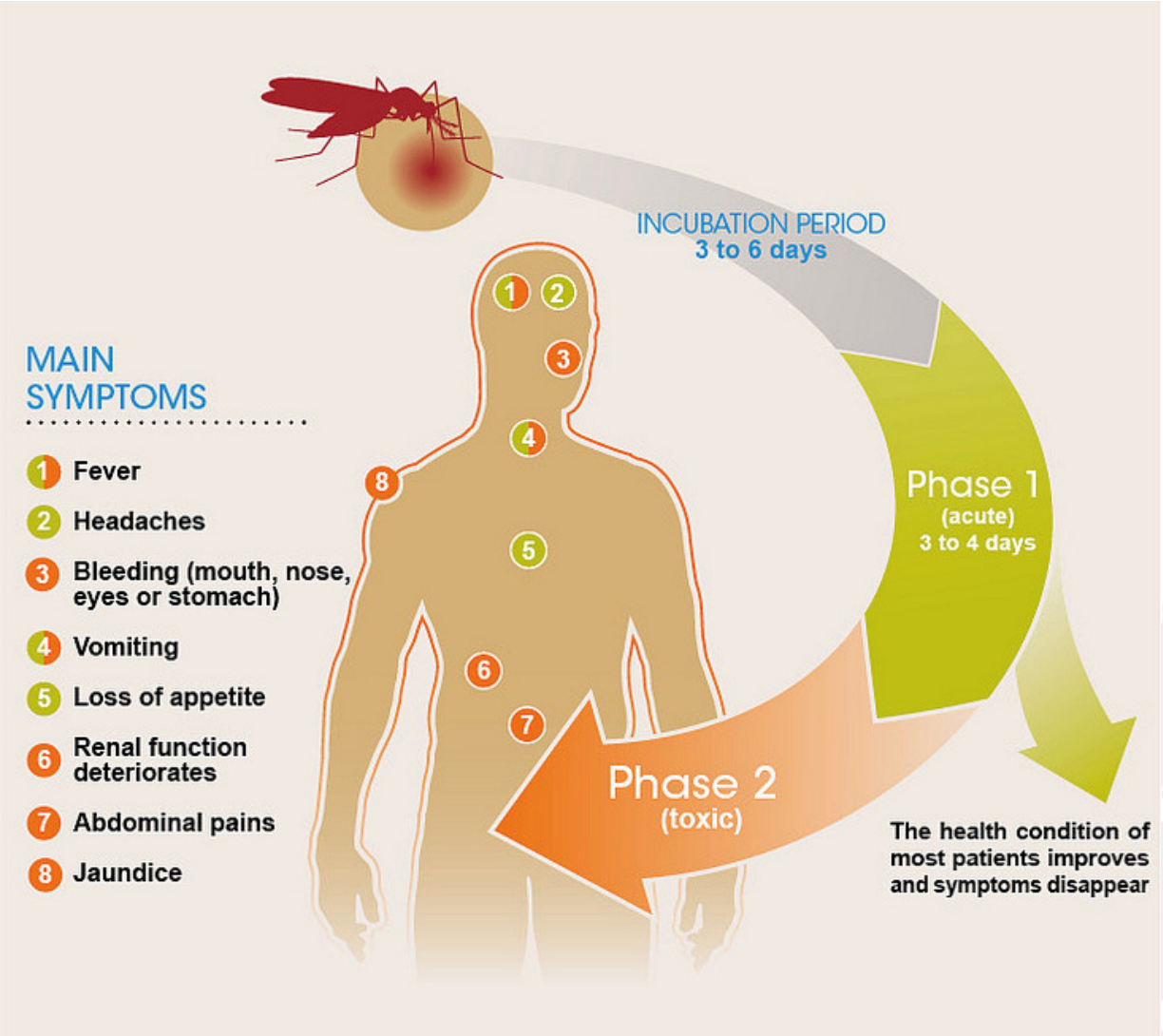


OXFORD UNIVERSITY PRESS

# YFV transmission cycles



# Yellow fever clinical picture

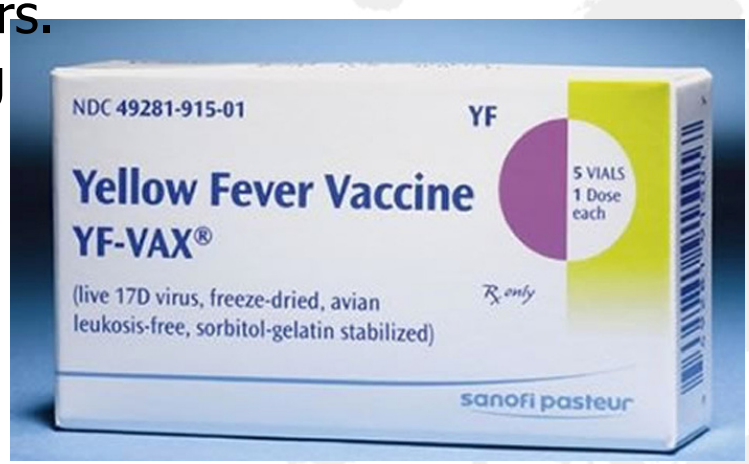


# Treatment and vaccination

- specific treatment not available
- attenuated vaccine, known as YF 17D,
  - safe, effective and inexpensive
  - has been used for more than half a century,
  - routine vaccination is implemented by very few countries,

**Travel to endemic countries > YF vaccination certificate**

A booster is required every ten years. There are some concerns regarding the risks and benefits of primary YF vaccination particularly for travellers over 60 years of age.



# Resurgence of Yellow fever in South America

- relatively low vaccine coverage in the outbreak areas,
- migration of susceptible individuals to forested regions where the disease is transmitted, and
- increasing urbanization of the disease.

# Yellow fever risk of transmission through SoHO

As only 15% - 25% of YF infected individuals develop symptoms, asymptomatic donors may donate infectious blood and potentially cell, tissues and organs.

YFV survives in blood preserved with citrate for 35 days and for 60 if preserved with glycerol

YF transmission through donated blood has not been documented but the risk cannot be excluded.

Yellow fever 17D vaccine has been transmitted through transfusion of blood donated by recently immunized donors .

# Yellow fever risk of transmission through SoHO

Prospective SoHO donor with a history of YF may donate :

- 14 days after full recovery from YF, afebrile and asymptomatic on the day of donation;
- 4 weeks after vaccination with attenuated viral vaccine;

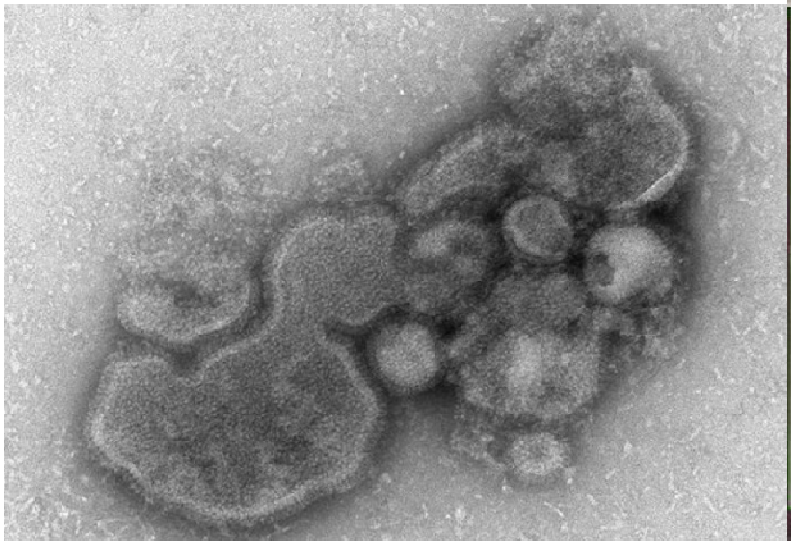
Deferral of donors returning from areas affected by malaria will be sufficient to prevent the donation of YF infected blood, tissues and cells.

# Yellow fever risk of transmission through SoHO

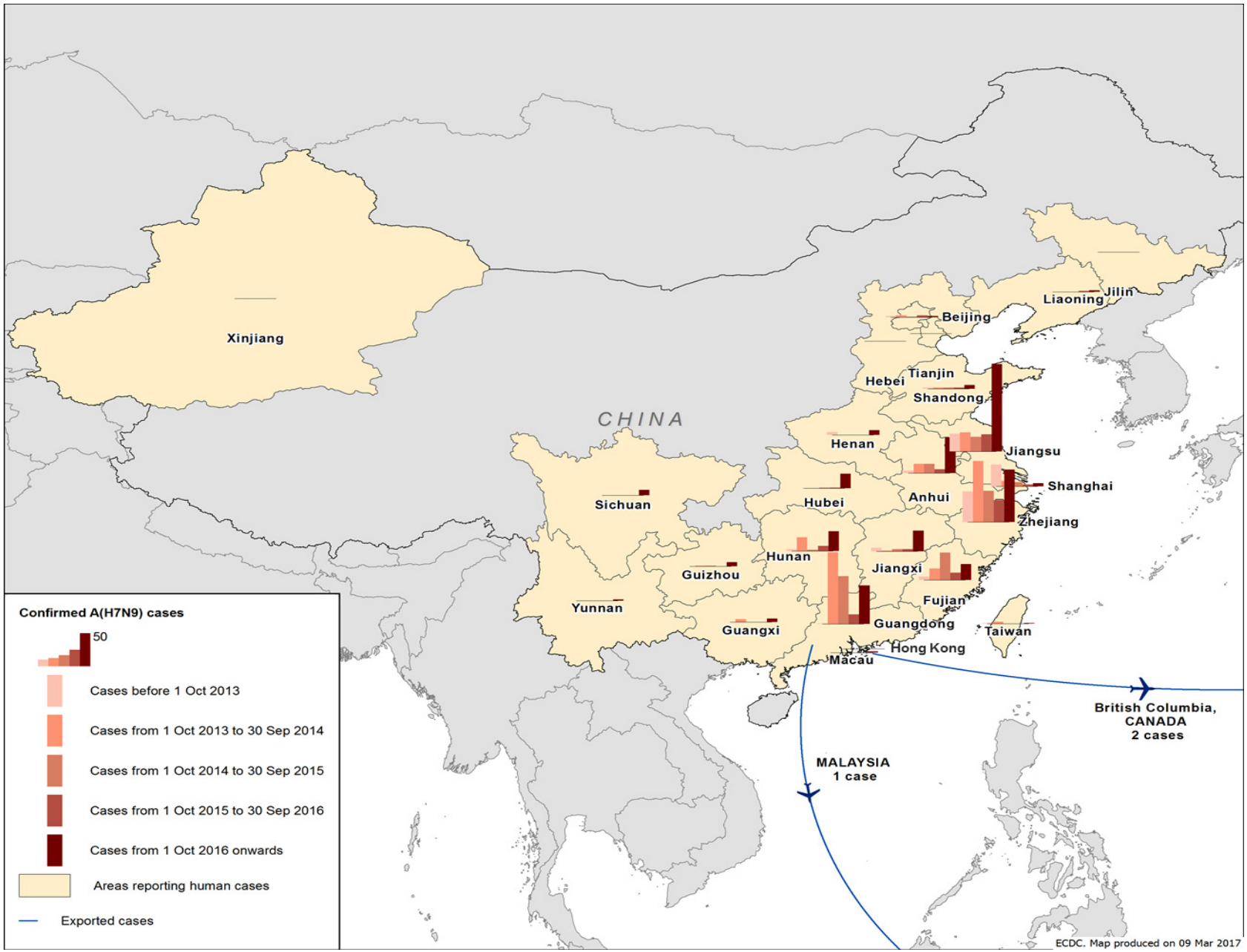
YF vaccination is contraindicated for immunocompromised patients after solid organ and haematopoietic stem cell transplantation. Patients living in countries endemic for yellow fever, or patients planning to travel to endemic countries in the future (work, leisure) should be immunised before transplantation.

# Influenza A(H7N9) Virus in China

On 31 March 2013, a novel A(H7N9) influenza virus isolated from three unlinked fatal cases of severe respiratory disease in eastern China, two in Shanghai and one in Anhui province of China.

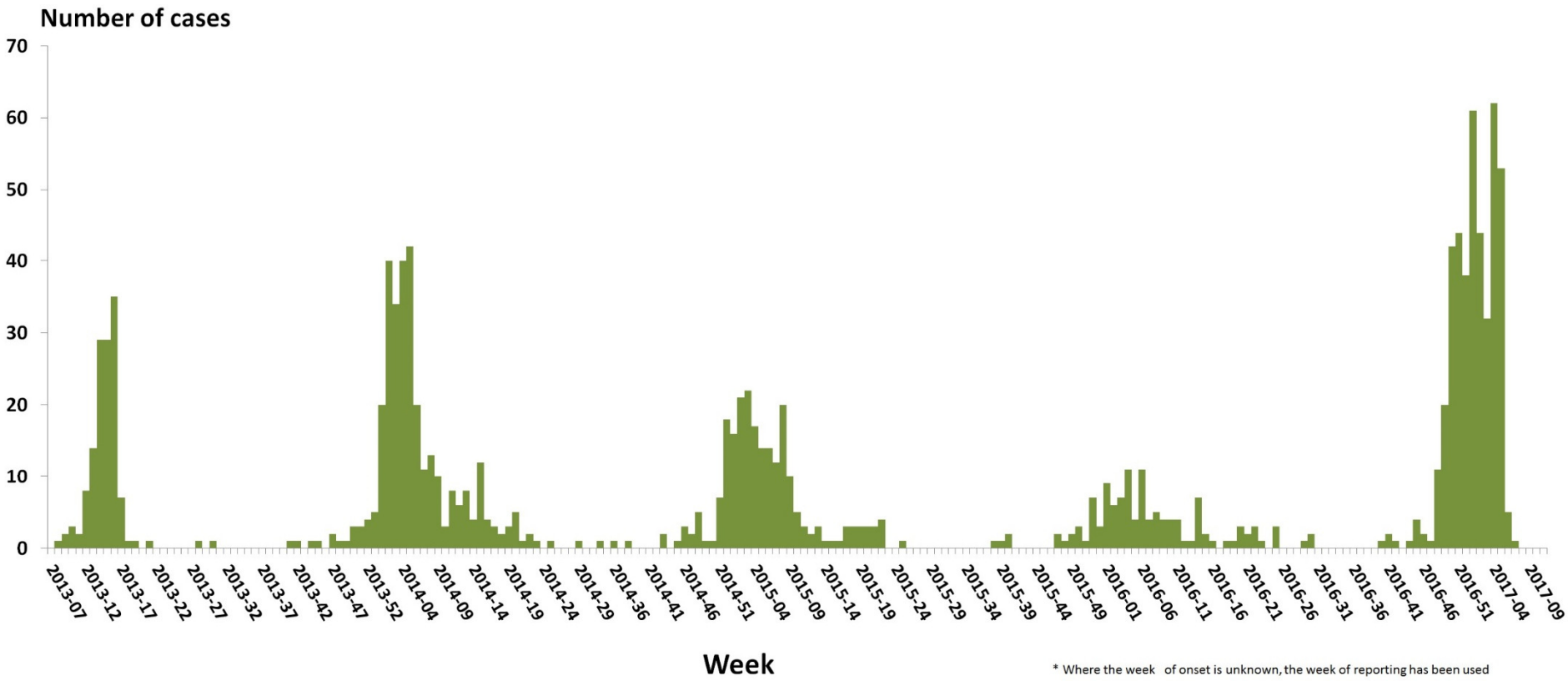


**Distribution of confirmed cases of A(H7N9) by five periods (weeks 7-2013 to 10-2017)**




**Source: European Centre for Disease Prevention and Control. Communicable Disease Threats Report, week 10. Stockholm: ECDC; 2017**

**Distribution of confirmed cases of A(H7N9) by first available week, February 2013 to 8 March 2017**




* Where the week of onset is unknown, the week of reporting has been used

**Source: European Centre for Disease Prevention and Control. Communicable Disease Threats Report, week 10. Stockholm: ECDC; 2017**

# Transmission of H7N9 infection through SoHO

Currently no specific guidance or standard exists for donor deferral related to infection with H7N9 influenza virus. Incubation period and ratio between symptomatic and asymptomatic disease for H7N9 virus infection are unknown.

It is assumed that the onset of, and subsequent subsidence of, the major symptoms and viremia tend to closely co-incide.

According to experiences with the H5N1 virus infection anticipated risk for transmission of the virus through transfusion and transplantation appeared to be low

# Zika virus infection (World) - update

26 October 2016 and 2 February 2017:

- epidemic appears to be slowing down in the Americas and the Caribbean regions
- 3/70 countries - mosquito-borne Zika virus transmission (3 new countries, Palau, Montserrat and Angola);
- 1/13 countries - sexual transmissions; (the UK one new case);
- 6/29 countries - microcephaly and other CNS malformations (6 new: Argentina, Bolivia, Guadeloupe, Nicaragua, Trinidad and Tobago and Vietnam);
- 2/22 countries - Guillain-Barré syndrome, (Bolivia and Saint Martin, at least one new case)

**Source: European Centre for Disease Prevention and Control. Communicable Disease Threats Report, week 7. Stockholm: ECDC; 2017**

# Zika virus infection (EU/EEA continental) - update

No locally acquired cases by vector-borne transmission

Since week 26/2015,

- 21 countries have reported 2 107 travel-associated Zika virus infections (TESSy). (most frequent France - 54%, Spain 15% and the UK 9%).
- 9 countries reported 107 Zika cases among pregnant women.

As of 3 February 2017,

- 6 countries reported 20 sexual transmission events, all from male partners to females where gender was reported: France (12), Italy (2), Netherlands (2), Spain (2), Portugal (1) and the United Kingdom (1).

Source: European Centre for Disease Prevention and Control. Communicable Disease Threats Report, week 7. Stockholm: ECDC; 2017

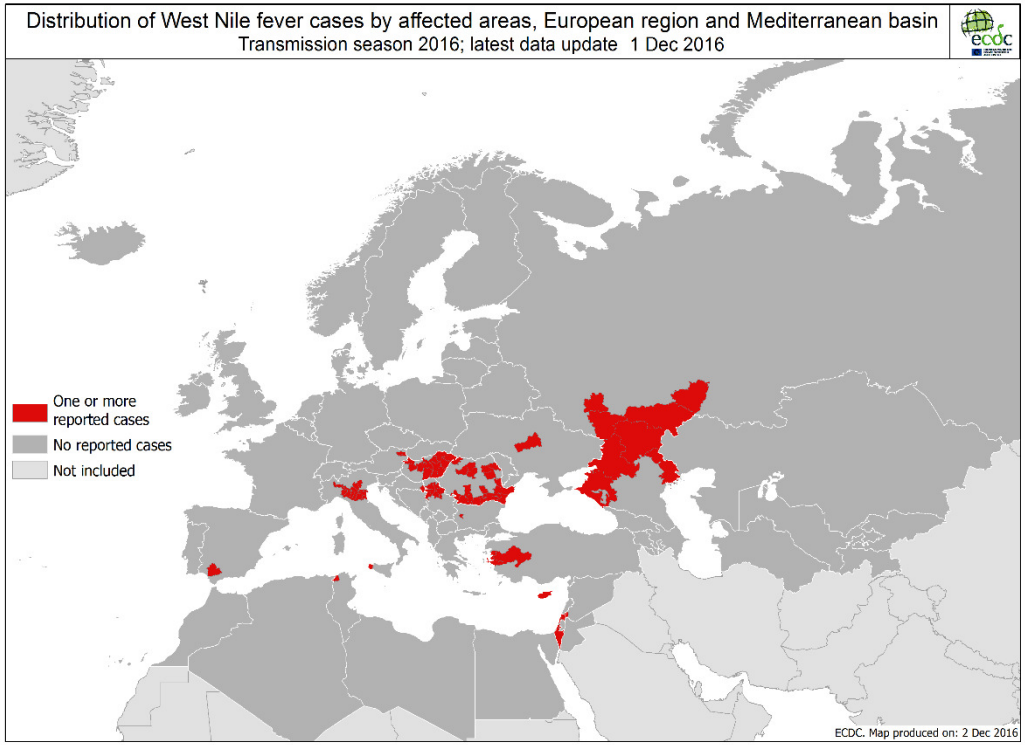
# Zika virus infection - update

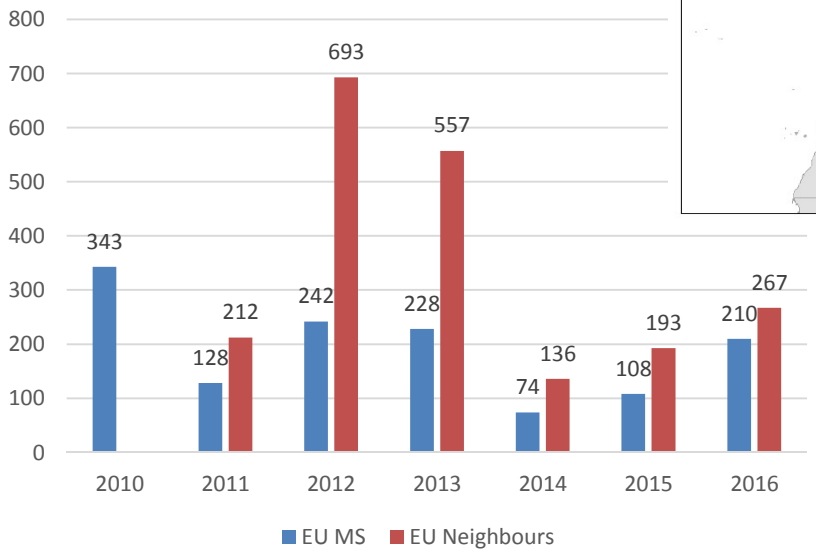
- A recent study (Martinique) - 75 viraemic blood donors 34 (45.3%) remained asymptomatic; 41 (54.7%) reported symptoms
- Previous reports - 80% of ZIKV infection cases - asymptomatic,
  - Ratio of asymptomatic/symptomatic infections may vary according to local conditions and Zika virus strain
  - A likelihood of SoHO donation by asymptomatic infectious donors may be lower than is currently estimated.
- In cooperation with the Working group of experts from EU/EEA Member States, ECDC is currently updating the scientific advice "Zika virus and safety of substances of human origin - A guide for preparedness activities in EU".
- The update covers the risk of Zika virus infection in SoHO donors exposed through sexual contact and changes in the ECDC's country classification.

**Source: European Centre for Disease Prevention and Control. Communicable Disease Threats Report, week 7. Stockholm: ECDC; 2017**

# Reported cases of West Nile fever for EU and neighbouring countries 2010 - 2016


*Culicidae spp.*




| Type of SoHO | Transmission |
|---|---|
| Cells & Tissues | + |
| Organs | + |
| Blood & blood comp. | + |

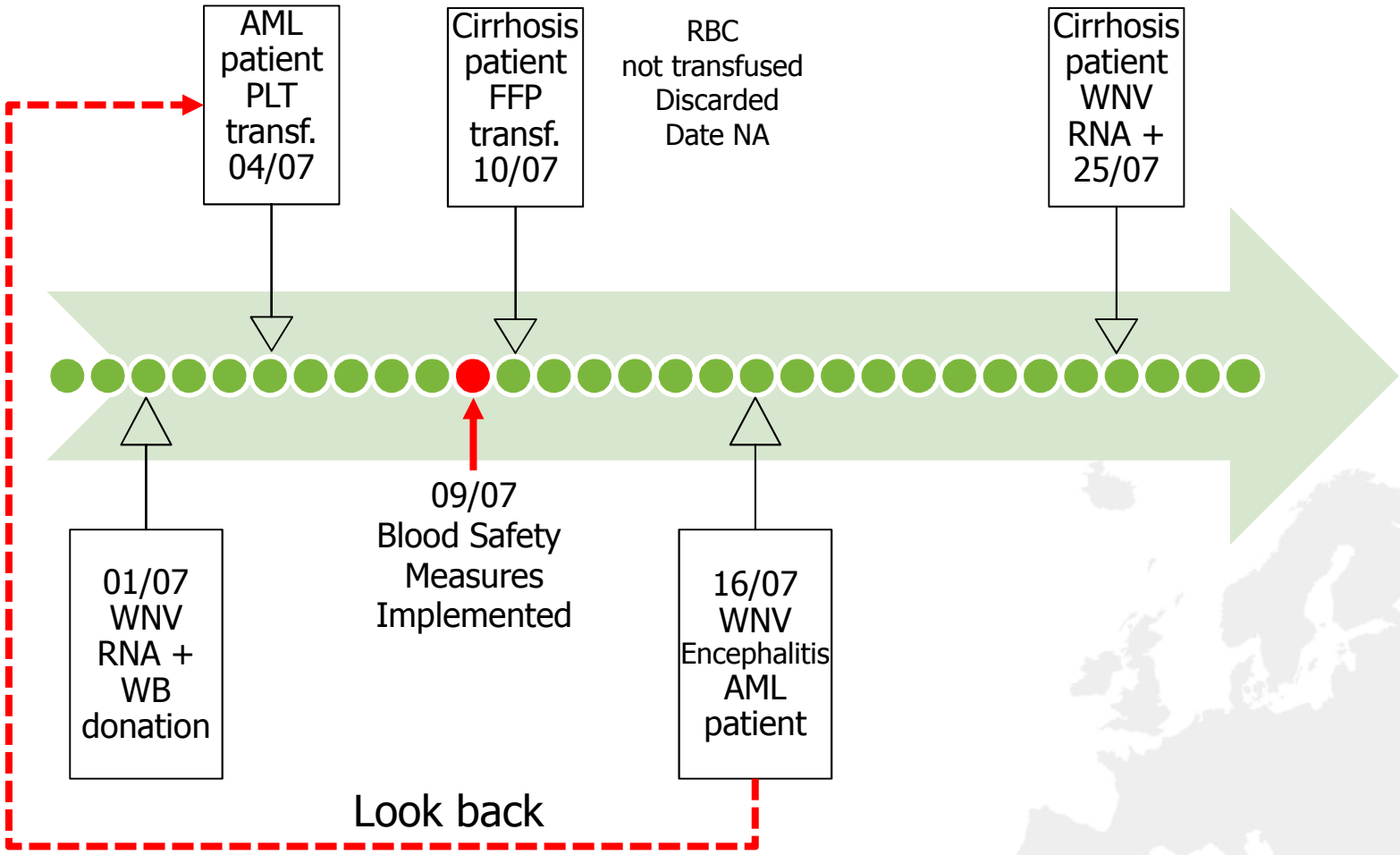
# WEST NILE VIRUS

**(published reports)**

| | | Bone | Bone Cortical | Bone Cancellous | Cornea | Epidermis | Erythrocytes | Heart Valves | Kidney | PBSC | Sperm | Unspecified | **Total** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Transmission(s) Proven | 2 | 1 | 1 | 1 | 1 | 5 | 3 | 12 | 2 | 1 | 4 | **33** |
| | | | | | | | | | | | | | |
| | Screening | 1 | 0 | 0 | x | x | 6 | 1 | 6 | 3 | 1 | 4 | **22** |
| | Screening PM | 0 | 0 | 0 | 0 | 1 | x | 1 | 3 | x | x | 1 | **6** |
| PS | Antibiotic Treatment | 0 | 0 | 0 | 0 | 0 | x | 1 | 0 | x | x | 0 | **1** |
| | Cultured | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | **1** |
| | Enzyme / Chemical Treatment | 4 | 3 | 3 | 0 | 1 | 1 | 0 | x | 0 | x | 2 | **14** |
| | Filtration / Centrifugation / Purification | 0 | 0 | 0 | x | x | 1 | x | x | 1 | 0 | 0 | **2** |
| | Irradiation Gamma/ E beam | 5 | 3 | 1 | x | 1 | 1 | x | x | 0 | x | 0 | **11** |
| | Washing | 1 | 1 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | **5** |
| SC | Freeze Dried | 2 | 1 | 1 | x | 0 | x | x | x | x | x | 0 | **4** |
| | Preservation Fluids | X | x | x | 0 | x | 1 | 0 | 1 | 1 | 0 | 1 | **4** |
| | Storage Temperature | 3 | 0 | 0 | 0 | 1 | 2 | 3 | 1 | 1 | 2 | 0 | **13** |
| TC | Donation Living / PM | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 1 | 0 | 1 | 0 | **4** |
| | Fluids Body / Blood | 1 | 0 | 0 | x | x | 0 | 0 | 0 | 0 | 0 | 0 | **1** |
| | Viable Cells | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | **0** |
| | **Total** | **19** | **9** | **7** | **1** | **5** | **20** | **9** | **24** | **9** | **5** | **13** | **121** |

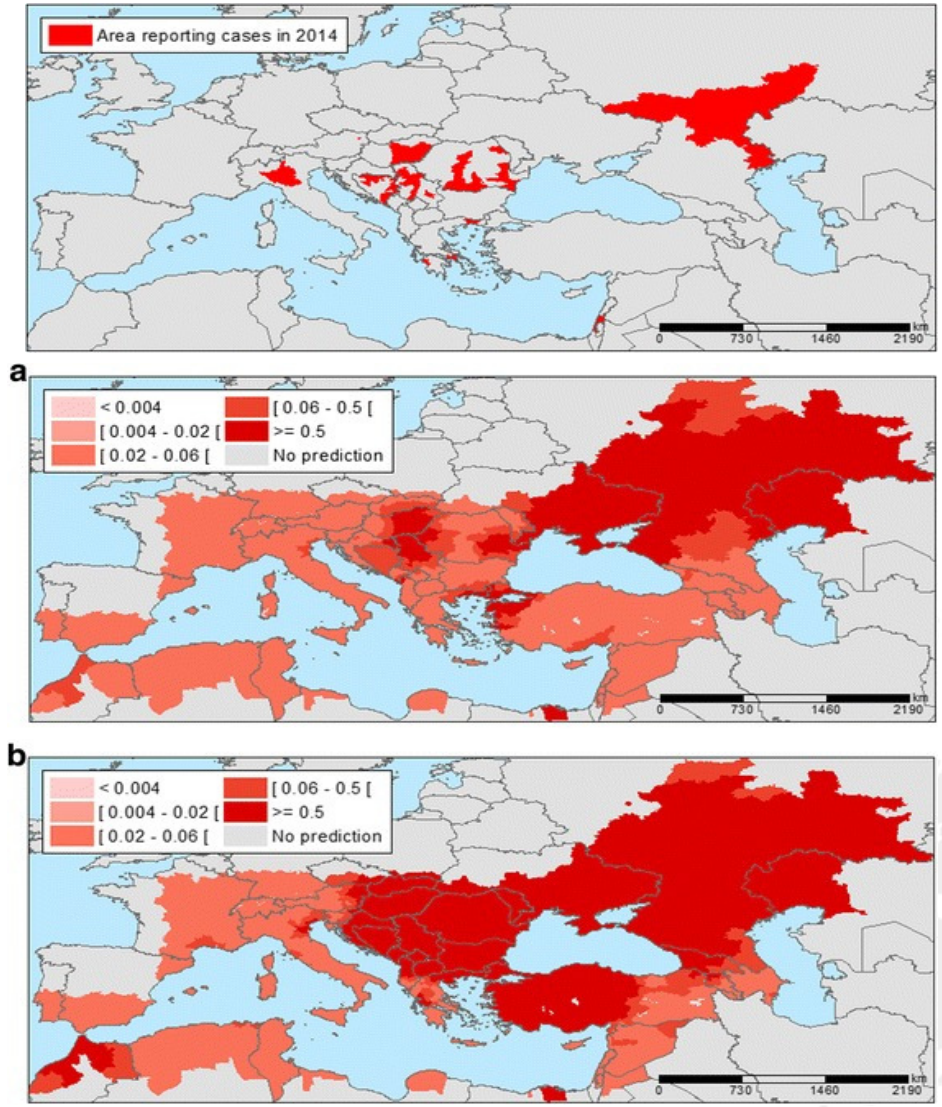
PS = Procedure Steps; SC = Storage Conditions; TC = Tissue Characteristics, Green: on WNV; yellow = another enveloped virus, white = not applicable (not necessary), red = missing data (x = not applicable)

# Cases of TT WNV infection - Greece 2012




Source: KeepIno Greece report 2012

# Predicted probability of districts with West Nile Virus infections based on July temperatures




2014

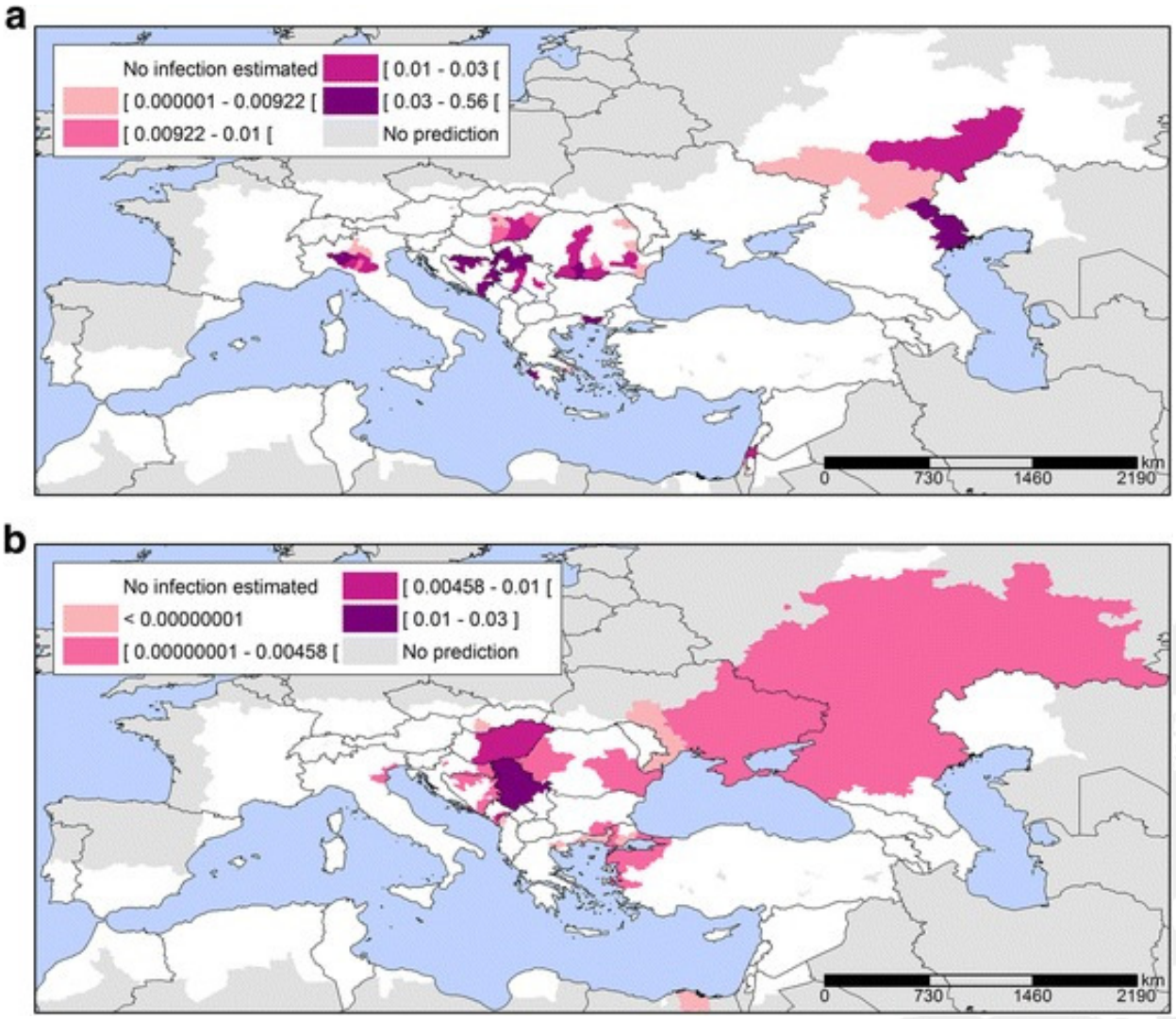
2025

2050

Semenza J et al. Environ Health. 2016; 15(Suppl 1): 28.

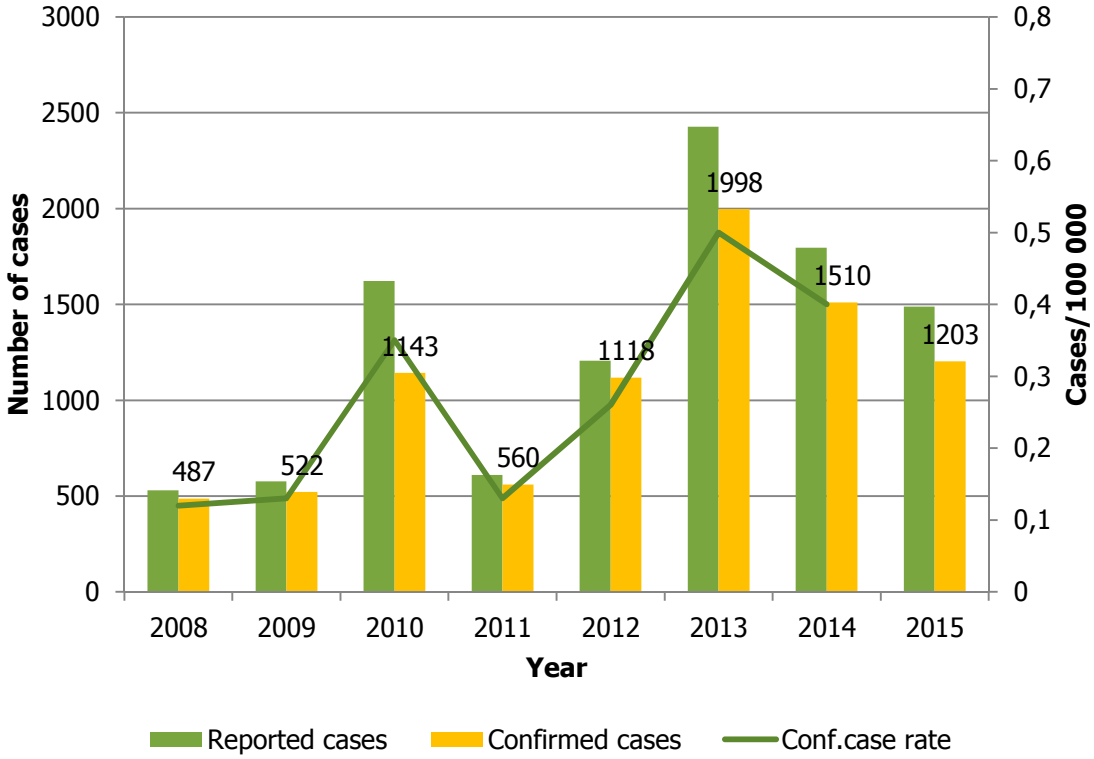
# Prediction

Estimated prevalence of West Nile Virus infections in the blood donor population (per 100,000) by district

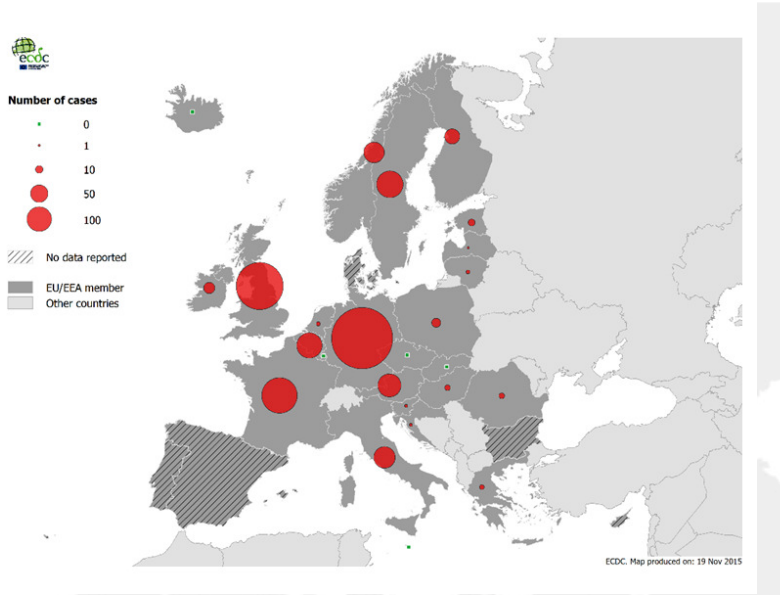



Semenza J et al. Environ Health. 2016; 15(Suppl 1): 28.

# Dengue
# Number and rate of reported cases




Locally acquired cases
France
4 cases 2014
1 case 2013
1 case (travel Madeira) 2013



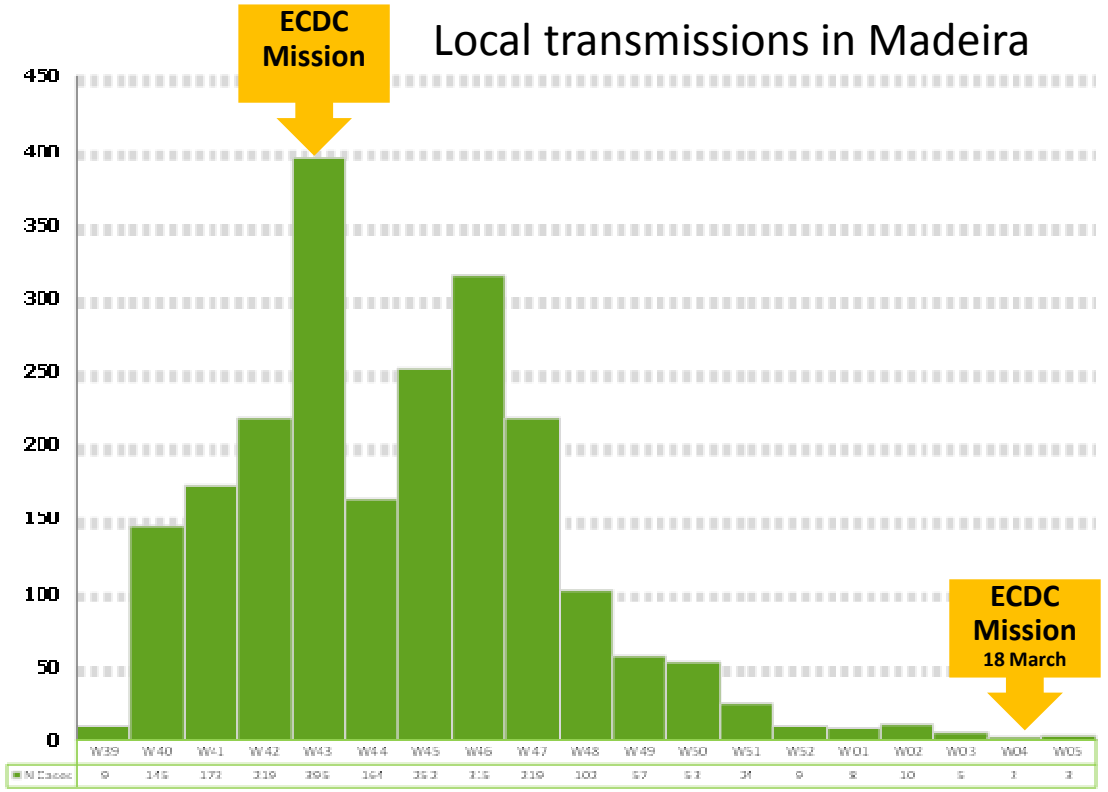

Overall case rate (2014): 0.4 /100 000

Source: Country reports from Austria, Belgium, Croatia, the Czech Republic, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Romania, Slovakia, Slovenia, Sweden, the United Kingdom.

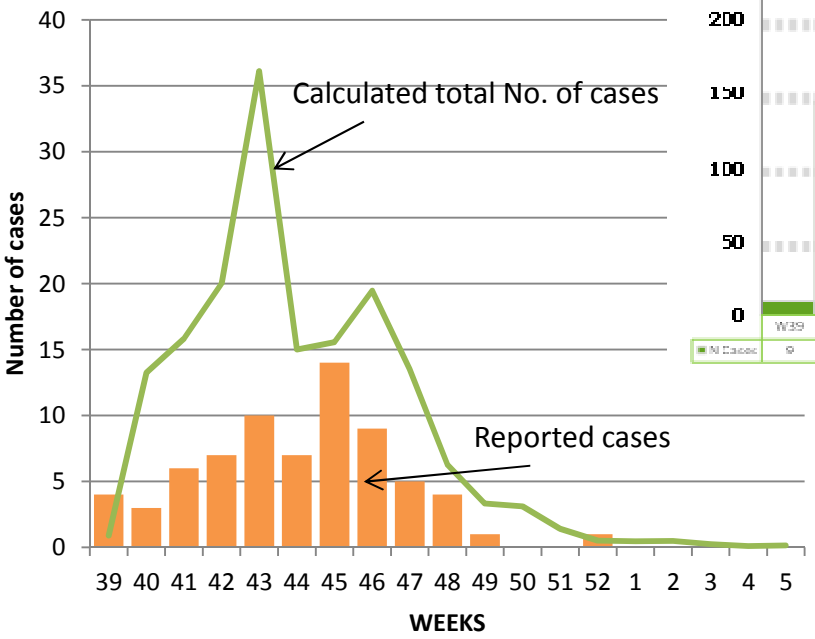
# Incidence of probable and confirmed cases of dengue in Madeira

Start: October 2012 –March 2013
Indigenous Cases reported: 2164

Local transmissions in Madeira

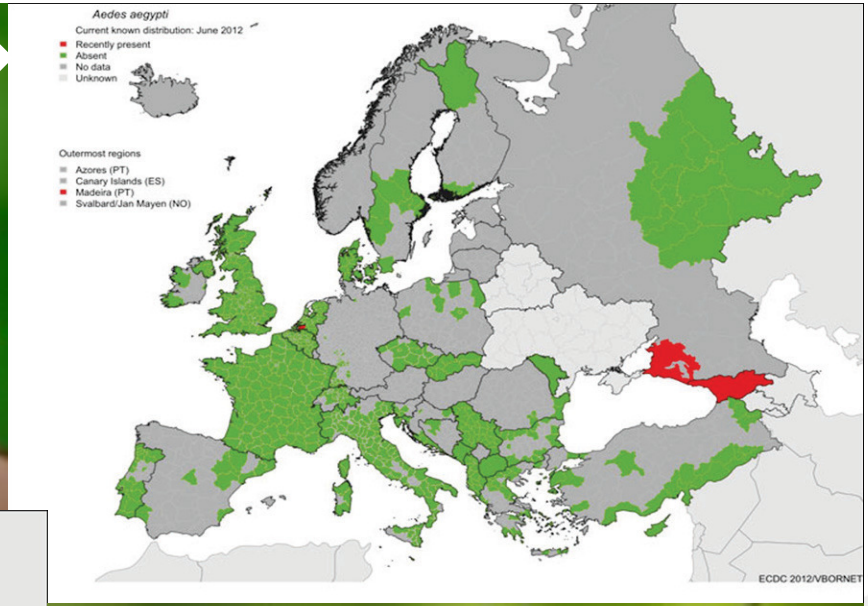


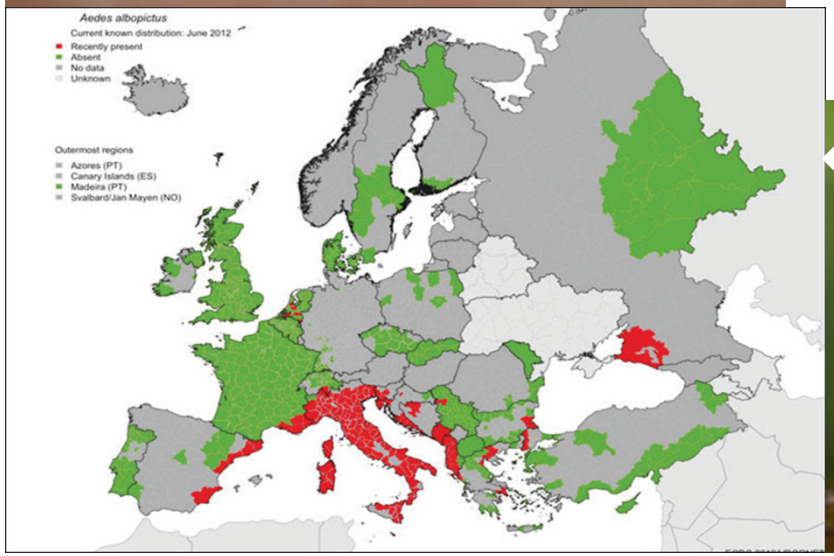

Imported cases from Madeira




Imported cases travellers from Madeira (78):
Portugal-11; UK – 23; Germany – 19; France 3; Sweden 5; Finland – 7; Poland - 2; Austria – 2; Norway – 2; Croatia – 1; Slovenia – 1;Spain – 1; Switzerland 1.

# Dengue – vectors & distribution June 2012

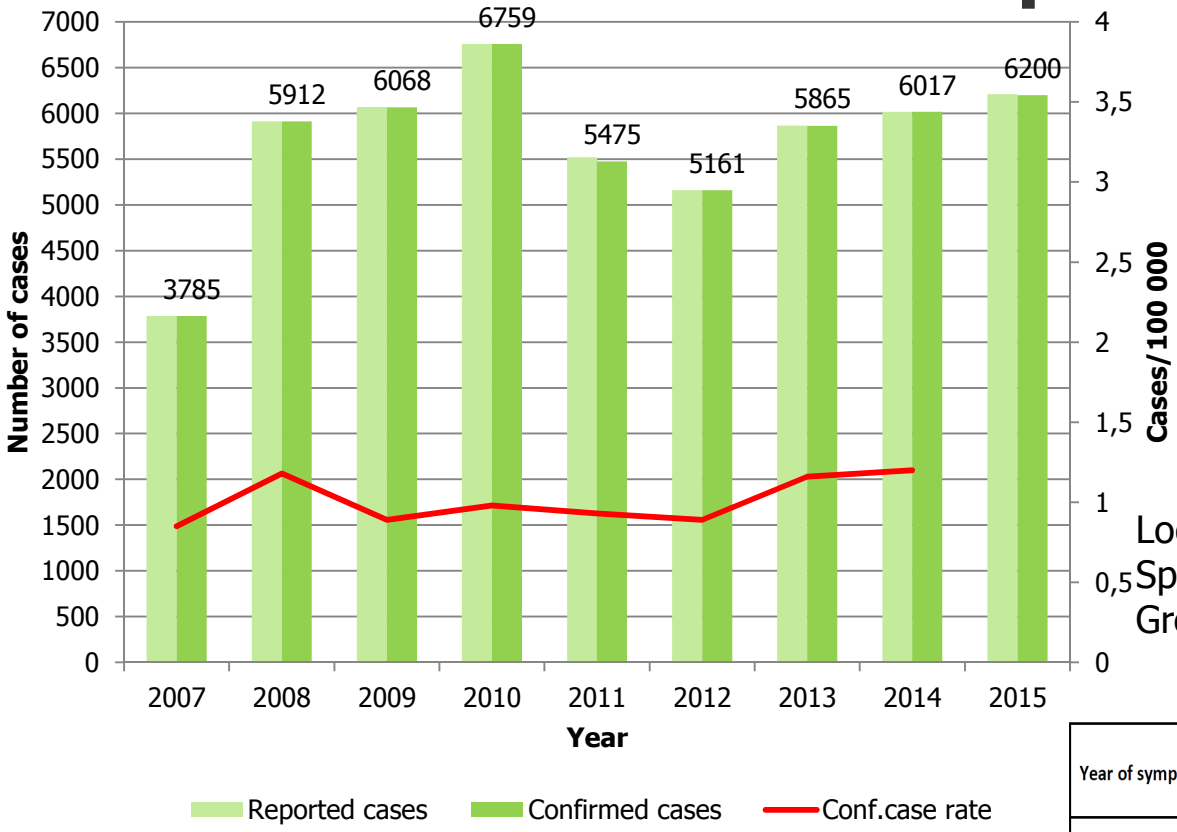



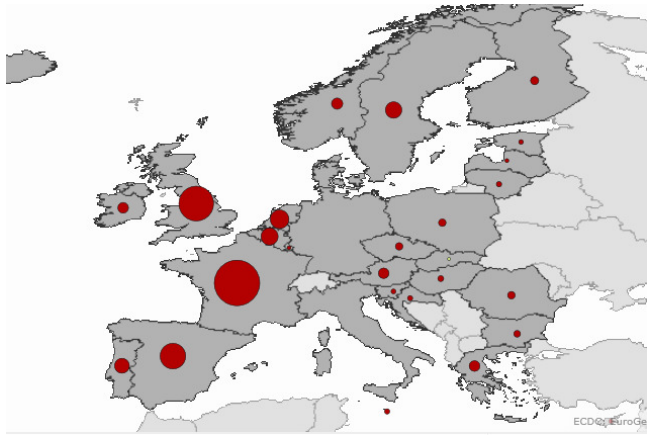




| | **DENGUE** (published reports) | Bone | Bone Cortical | Bone Cancellous | Cornea | Epidermis | Erythrocytes | Heart Valves | Kidney | Peripheral Blood SC | Sperm | Unspecified | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Transmission(s) Proven | 4 | 2 | 2 | 7 | 4 | 2 | 1 | 9 | 1 | 3 | 5 | **40** |
| | | | | | | | | | | | | | |
| | Screening | 1 | 0 | 0 | x | x | 5 | 1 | 1 | 3 | 2 | 1 | **14** |
| | Screening PM | 0 | 0 | 0 | 0 | 1 | x | 1 | 1 | x | x | 1 | **4** |
| PS | Antibiotic Treatment | 0 | 0 | 0 | 0 | 0 | x | 1 | 0 | x | x | 0 | **1** |
| | Cultured | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | **1** |
| | Enzyme / Chemical Treatment | 4 | 3 | 3 | 0 | 1 | 1 | 0 | x | 0 | X | 1 | **13** |
| | Filtration / Centrifugation / Purification | 0 | 0 | 0 | x | x | 1 | x | x | 1 | 0 | 0 | **2** |
| | Irradiation Gamma/ E beam | 5 | 3 | 1 | x | 1 | 3 | x | x | 0 | x | 0 | **13** |
| | Washing | 2 | 1 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | **6** |
| SC | Freeze Dried | 2 | 1 | 1 | x | 0 | x | x | x | x | x | 0 | **4** |
| | Preservation Fluids | X | x | x | 0 | x | 2 | 0 | 1 | 1 | 0 | 1 | **5** |
| | Storage Temperature | 3 | 0 | 0 | 0 | 1 | 2 | 1 | 1 | 1 | 2 | 0 | **11** |
| TC | Donation Living / PM | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 1 | 0 | 1 | 0 | **4** |
| | Fluids Body / Blood | 1 | 0 | 0 | x | x | 0 | 0 | 0 | 0 | 0 | 0 | **1** |
| | Viable Cells | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | **0** |
| | Total | **22** | **10** | **8** | **7** | **8** | **19** | **5** | **14** | **8** | **8** | **10** | **119** |

PS = Procedure Steps; SC = Storage Conditions; TC = Tissue Characteristics; Green: on dengue; yellow = another enveloped virus, white = not applicable (not necessary), red = missing data; x = not applicable

# Malaria
# Number and rate of reported cases



Locally transmitted malaria:
Spain – 1 case (2014)
Greece: 6 cases (2015); 5 cases (2016)

**Overall case rate (2014): 1.2 / 100 000**

Source: Country reports from Austria, Cyprus, Czech Republic, Estonia, Finland, Germany, Greece, Hungary, Ireland, Malta, Netherlands, Norway, Poland, Portugal, Slovakia, Slovenia, Spain, Sweden and United Kingdom

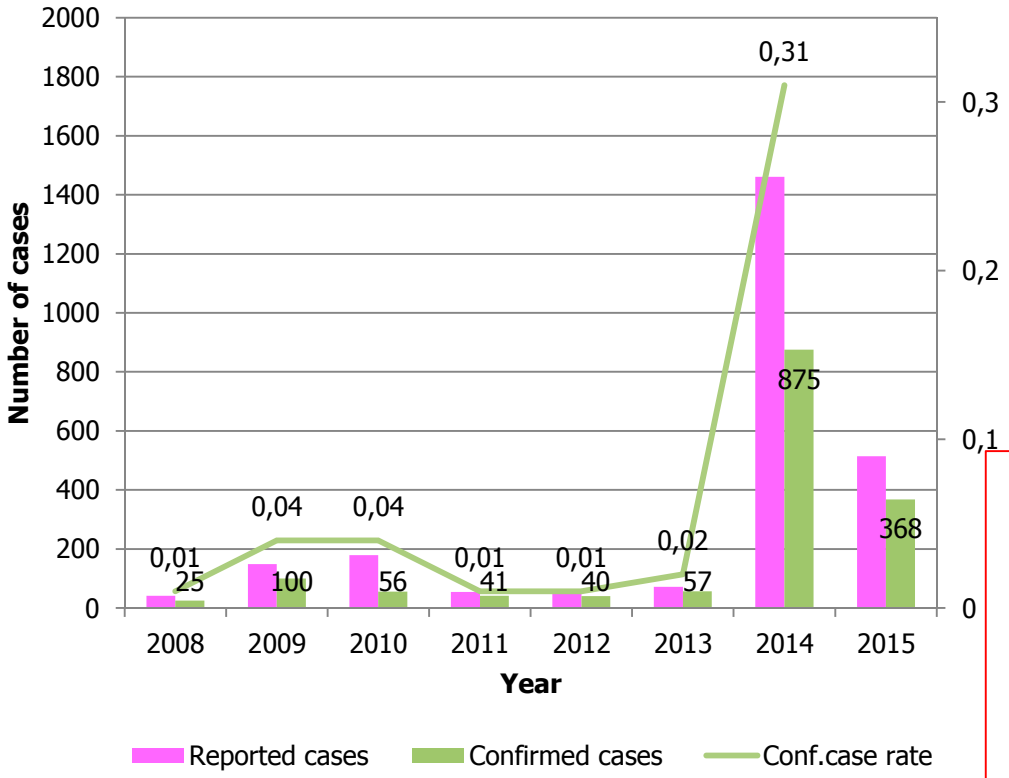
Malaria cases in Greece 2009 - 2014

| Year of symptom onset | Case classification | | Total |
|---|---|---|---|
| | Imported cases | Locally-acquired cases[2] | |
| 2009 | 44 | 7 | 51 |
| 2010 | 40 | 4 | 44 |
| 2011 | 54 | 42 | 96 |
| 2012 | 73 | 20 | 93 |
| 2013 | 22 | 3 | 25 |
| 2014 | 38 | 0 | 38 |

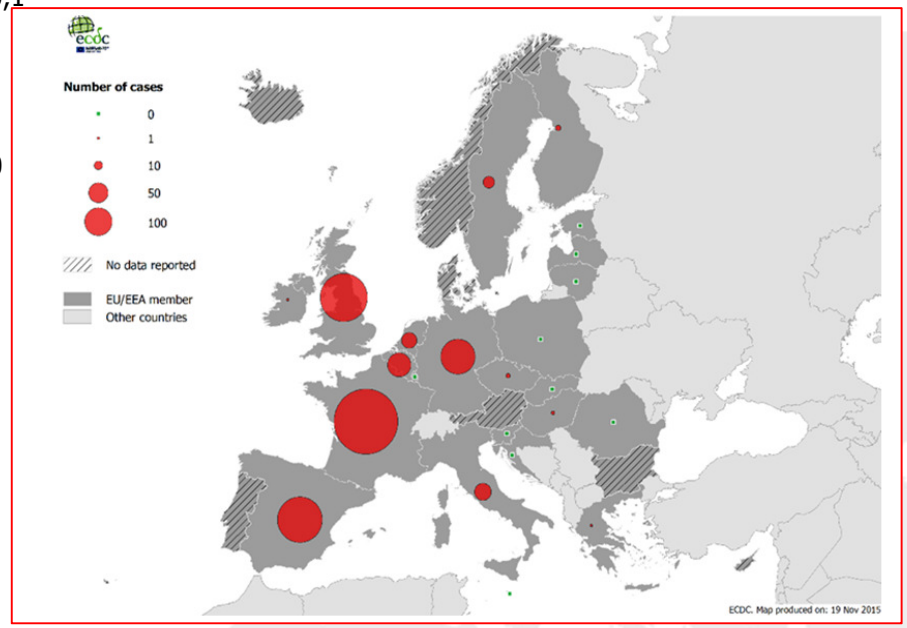
| | **MALARIA** (published articles) | Bone | Bone Cortical | Bone Cancellous | Cornea | Epidermis | Erythrocytes | Heart Valves | Kidney | Peripheral Blood SC | Sperm | Unspecified | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Transmission(s) Proven | 1 | 0 | 4 | 1 | 0 | 1 | 1 | 18 | 6 | 0 | 0 | **32** |
| | | | | | | | | | | | | | |
| | Screening | 0 | 0 | 0 | x | x | 2 | 0 | 2 | 1 | 0 | 0 | **5** |
| | Screening PM | 0 | 0 | 0 | 0 | 0 | x | 0 | 1 | x | x | 0 | **1** |
| PS | Antibiotic Treatment | 0 | 0 | 0 | 0 | 0 | x | 0 | 0 | x | x | 0 | **0** |
| | Cultured | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | **0** |
| | Enzyme / Chemical Treatment | 0 | 0 | 0 | 0 | 0 | 0 | 0 | x | 0 | x | 0 | **0** |
| | Filtration / Centrifugation / Purification | 0 | 0 | 0 | x | x | 2 | x | x | 0 | 0 | 0 | **2** |
| | Irradiation Gamma/ E beam | 0 | 0 | 0 | x | 0 | 1 | x | x | 0 | x | 0 | **1** |
| | Washing | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | **0** |
| SC | Freeze Dried | 0 | 0 | 0 | x | 0 | x | x | x | x | x | 0 | **0** |
| | Preservation Fluids | X | x | x | 0 | x | 0 | 0 | 0 | 0 | 0 | 0 | **0** |
| | Storage Temperature | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | **4** |
| TC | Donation Living / PM | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | **0** |
| | Fluids Body / Blood | 0 | 0 | 0 | x | x | 0 | 0 | 0 | 0 | 0 | 0 | **0** |
| | Viable Cells | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | **0** |
| | Total | **2** | **1** | **5** | **1** | **0** | **6** | **1** | **21** | **8** | **0** | **0** | **45** |

*PS = Procedure Steps; SC = Storage Conditions; TC = Tissue Characteristics ; green: on malaria; white = not applicable (not necessary), red = missing data, (x = not applicable)*

# Chikungunya
# Number and rate of reported cases




Reported cases = 1 461
Travel related=1406
Locally acquired =11 France, Unknown place of infection=44
20-fold increase compared with 2013.
France (550), United Kingdom (301), Spain (272), travelling to destinations with chikungunya outbreaks in 2014




**Overall case rate (2014): 0.31/100 000**

Source: Country reports from Belgium, Croatia, the Czech Republic, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Romania, Slovakia, Slovenia, Spain, Sweden, the United Kingdom.

# Chikungunya outbreak in the Caribbean 2014

| **Chikungunya (published articles)** | Bone | Cord Blood | Whole Blood | Erythrocytes | Platelets | Plasma | Organs | Kidney | Heart | Lung | Sperm | stem Cells | Bone Marrow | Cornea |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | | |
| Transmission | 0 | 1 | 1 | 1 | 1 | 1 | 2 | 1 | 0 | 0 | 0 | 1 | 1 | 0 |
| | | | | | | | | | | | | | | |
| Donor History | 0 | 0 | 7 | 1 | 1 | 1 | 2 | 1 | 0 | 0 | 0 | 1 | 1 | 0 |
| Enzyme/Chemical Treatment | 0 | 0 | 3 | 1 | 4 | 4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Filtration/Centrifugation/Purification | 0 | 0 | 0 | 0 | 0 | 1 | NA | NA | NA | NA | 0 | 0 | 0 | NA |
| Lab Screening | 0 | 0 | 10 | 1 | 2 | 1 | 2 | 1 | 0 | 0 | 0 | 1 | 1 | 2 |
| Radiation Gamma/E beam | 0 | NA | 3 | 1 | 4 | 3 | NA | NA | NA | NA | NA | NA | NA | NA |
| Storage Temp | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

# Instead of conclusion

” Blood transfusion is like marriage, it should not be entered upon lightly, unadvisedly or wantonly, or more often than is absolutely necessary”

Beal R, 1976