



A EUROPEAN PERSPECTIVE ON EMERGING INFECTIONS

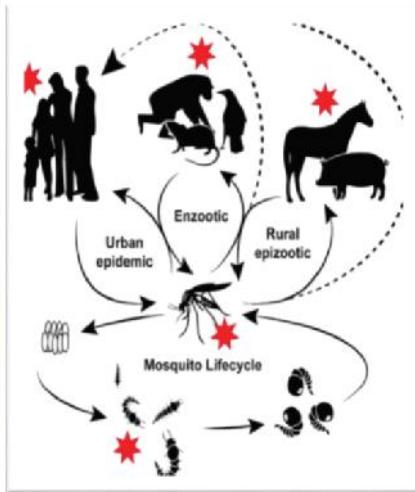
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Sanquin Blood Supply, Donor Medicine Research

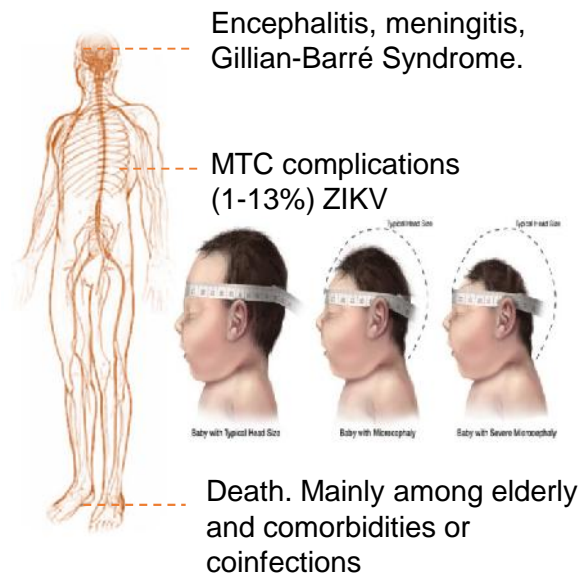
CONTENTS

- Background
- Objectives
- Methodology
- Results
- Conclusions

ARBOVIRUS INFECTIONS



Biological complexity
of their transmission
pattern (different
vectors, reservoirs)

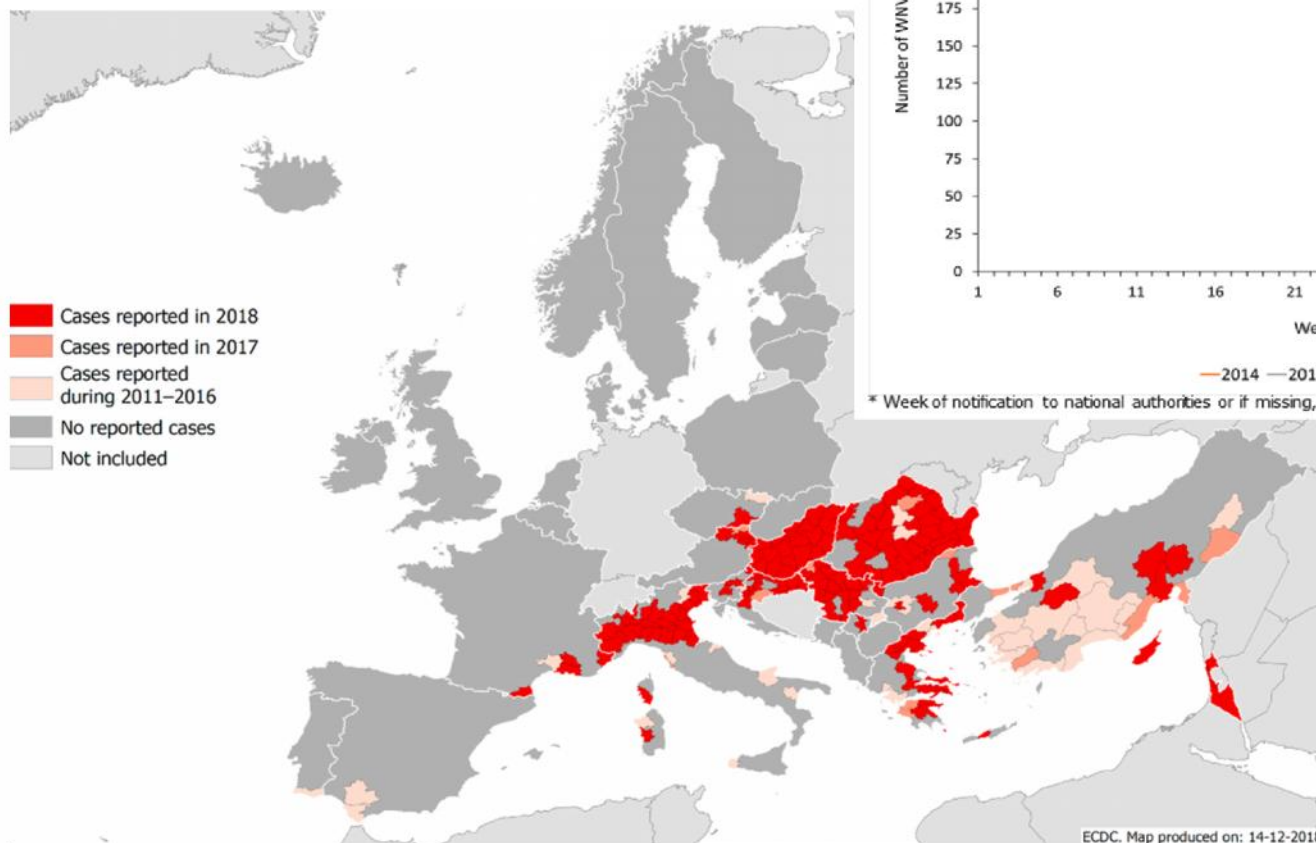


Impact of
serious complications

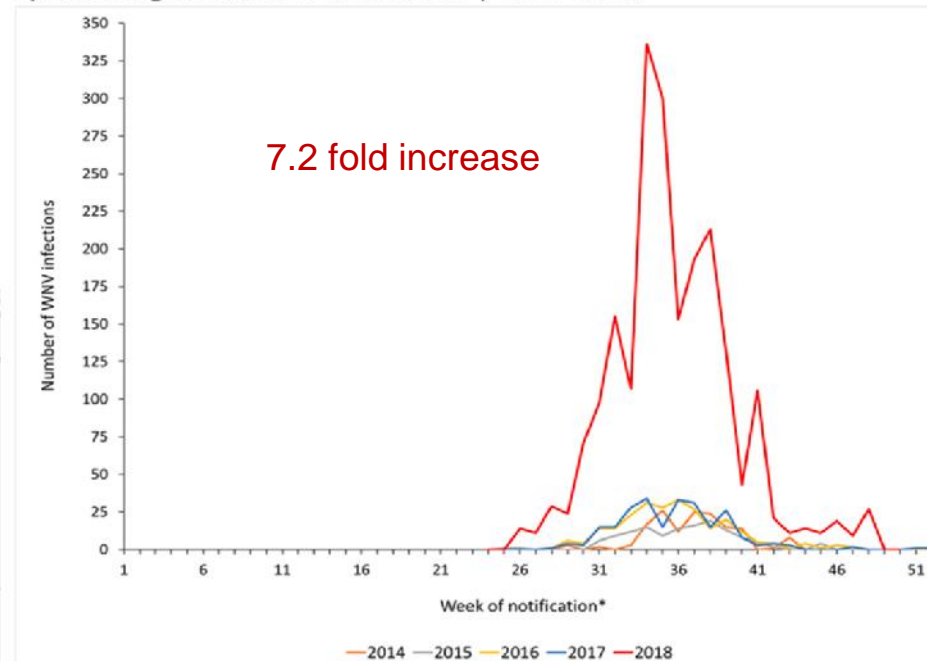


Epidemiological potential
(**mobility** of infected **travellers**
and establishment and **spread**
of **vectors** in new areas).

Spread of WNV in Europe



Number of WNV infections in EU/EEA and EU enlargement countries by epidemiological week of notification*, 2014-2018.



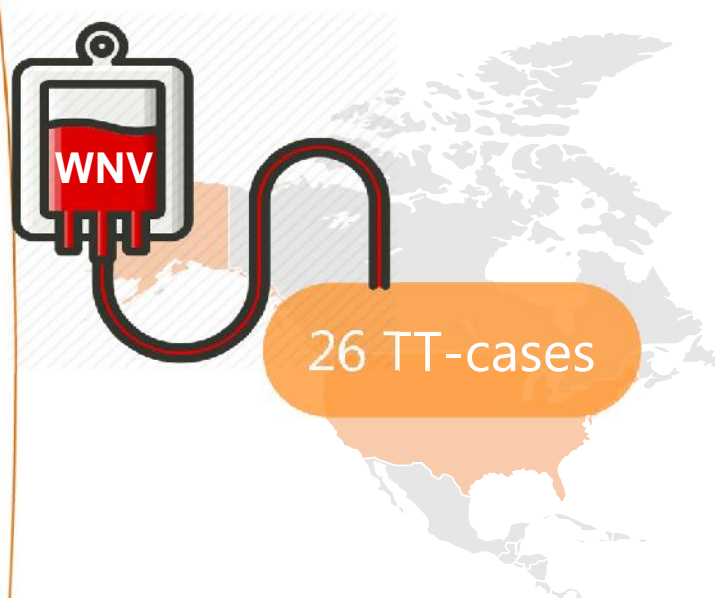
* Week of notification to national authorities or if missing, week of notification to ECDC.

<https://ecdc.europa.eu/en/west-nile-fever/surveillance-and-disease-data/disease-data-ecdc>

Distribution of West Nile virus infections in humans by affected areas in the EU/EEA Member States and EU neighbouring countries
Transmission season 2018 and previous transmission seasons; latest data update 13 Dec 2018



First WNV-TT in USA (2002)



- The presence of an **asymptomatic viremic phase** (80% completely asymptomatic)
- The ability of the infectious agent to **survive in collected** and processed **blood** or components
- The ability to **cause infection** and disease through **blood transmission**.



15
symptomatic



13
meningoencephalitis



2
fever



7
deaths

REGULATION AND RECOMMENDATIONS



Directive 2014/110/EU

Prospective blood donors should be **deferred for 28 days** after leaving an **area with evidence of WNV circulation** among **humans** unless the results of an **individual nucleic acid test** are negative.



Application of the **same policies/ recommendations** for donors returning from areas affected by **ZIKV** and **CHIKV**.

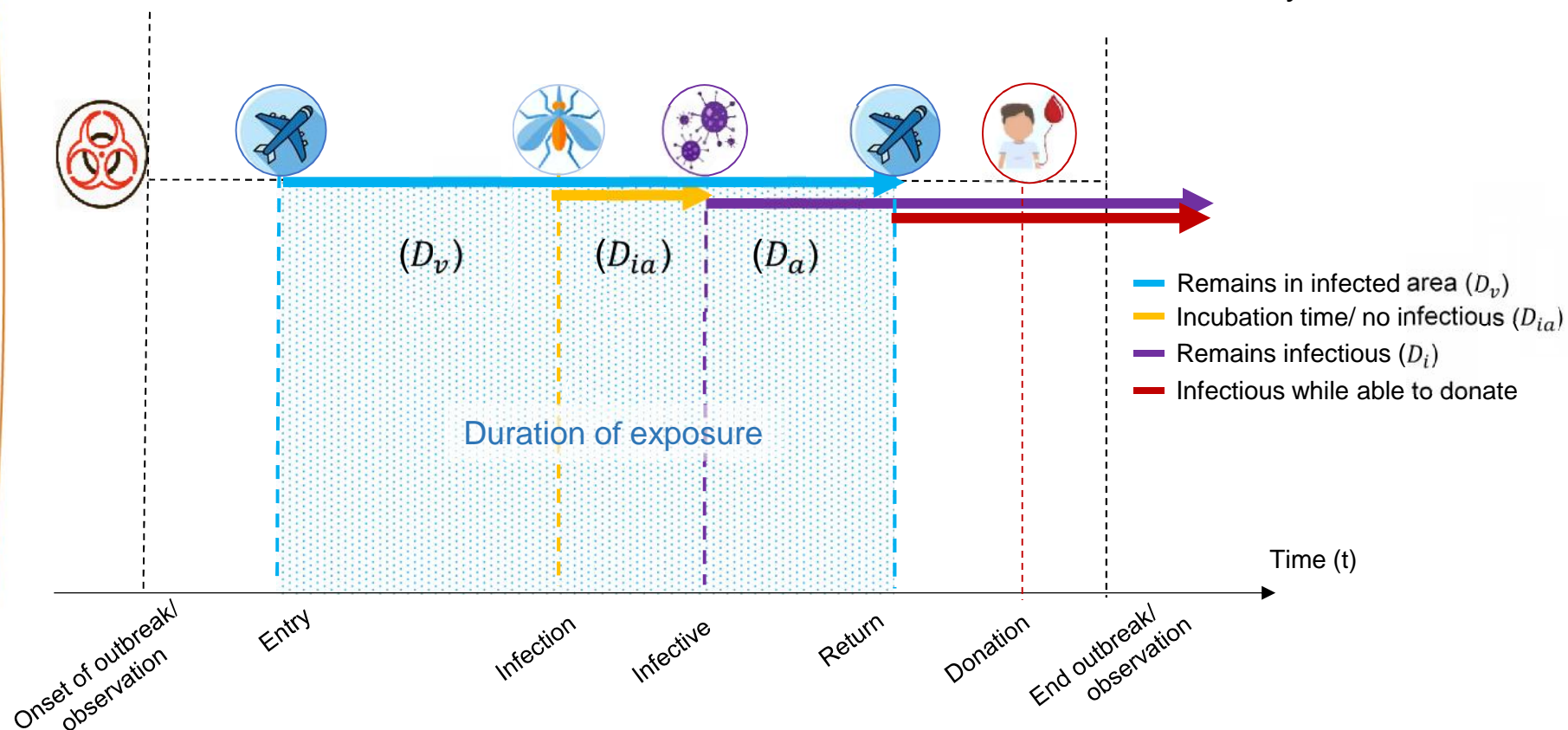
What is the **impact** that one of these outbreaks will generate for the **European blood safety**?

OBJECTIVES

- 1) Instead of analysing the risk of transmission by blood transfusion per individual country, estimate the **risk of emerging infection transmission throughout Europe**
- 2) Develop a **simple tool** to calculate the **combined risk of disease transmission** for outbreaks in specific countries/areas for **Europe as a whole**
- 3) Derive the number of **infections transmitted by blood transfusion throughout Europe** per observed infection in Europe (R_{0t})
- 4) This allows an easy, back-of-the-cigar-box estimate of the **impact of an outbreak** for the **European blood supply**

METHODOLOGY

Number of infected blood products from travelling donors after returning to their home country.



Conservative Estimate of the Number of Infectious Disease Transmissions by European Travelling Donors

$$n_i = \sum_j \left(\underbrace{p_{dj} \cdot \varphi_j}_{\text{donor icon}} \cdot \underbrace{\frac{f_{v,j,i}}{N_i}}_{\text{airplane icon}} \cdot \underbrace{\frac{(D_a/2 + D_{ia}) \cdot D_a}{1 - p_u}}_{\text{virus icon}} \right)$$

n_i = the number of infected blood products per observed infection in outbreak region i

p_{dj} = the **proportion of donors** of the general population in country j

φ_j = the number of **blood product distributed** per donor per day country j

$f_{v,j,i}$ = the number of **visitors per day** to the outbreak region i from country j

N_i = the number of **inhabitants** in the **outbreak region** i

D_a = the **duration of infectivity** of an infected donor (days)

D_{ia} = the **length of time** it takes for a donor to **become infectious** (days)

p_u = the proportion of **unobserved infections**

Risk model



European Up-Front Risk Assessment Tool (EUFRAT)

$$n_i = \sum_j \left(p_{dj} \cdot \varphi_j \cdot \frac{f_{v,j,i}}{N_i} \right) \cdot \frac{(D_a/2 + D_{ia}) \cdot D_a}{1 - p_u}$$

Data collection



Calculation

PARTNER	Netherlands	Norway	Poland	Portugal	Slovakia	Spain	Sweden	Switzerland and Liechtenstein	United Kingdom	Yugoslav	Country specific Travelling donors' risk factor (pd fv Phi / N)
Montenegro	5.77.E-09	6.33.E-09	3.16.E-08	1.46.E-09	6.43.E-09	2.28.E-09	9.35.E-09	6.96.E-09	2.06.E-08	0.00.E+00	2.83E-07
Netherlands	0.00.E+00	3.10.E-09	3.35.E-09	1.99.E-09	5.43.E-10	7.24.E-09	4.73.E-09	5.10.E-09	4.12.E-08	0.00.E+00	3.30E-07
Norway	2.36.E-08	0.00.E+00	8.70.E-09	1.13.E-09	1.25.E-09	1.04.E-08	6.69.E-08	8.17.E-09	2.74.E-08	0.00.E+00	3.83E-07
Poland	1.18.E-09	2.40.E-09	0.00.E+00	3.17.E-10	1.01.E-09	1.52.E-09	2.54.E-09	4.75.E-10	4.23.E-09	0.00.E+00	5.42E-08
Portugal	1.77.E-08	3.29.E-09	7.58.E-09	0.00.E+00	6.00.E-10	4.98.E-08	7.42.E-09	8.39.E-09	5.97.E-08	0.00.E+00	3.55E-07
Romania	9.15.E-10	3.19.E-10	1.92.E-09	2.62.E-10	4.61.E-10	1.35.E-09	5.33.E-10	4.44.E-10	2.41.E-09	0.00.E+00	3.53E-08
Slovakia	1.40.E-09	6.34.E-10	1.24.E-08	3.87.E-10	0.00.E+00	1.71.E-09	1.38.E-09	1.18.E-09	4.87.E-09	0.00.E+00	1.25E-07

RESULTS

European Travelling donors' risk assessment

(Grey cells are input fields)

Virus assessed

Select virus to assess (or select other)

Country assessed

Select country or region at risk to evaluate

Disease characteristics

Duration of latent period of acute infection (days)

Duration of infectious period during the acute phase of the disease (days)

Outbreak characteristics

European country of outbreak

Number of observed infections

Proportion of unobserved/ asymptomatic infections

Risk parameters

Country specific travelling donors' risk factor (per day)

Visitors per inhabitant per year

Disease specific travelling donors' risk factor (days squared)

Country specific local transmission risk factor (per day)

Estimated number of transmissions by blood products

In the country at risk (or for all of Europe if selected), per observed infection

In the country of the outbreak (or for all of Europe if selected), per observed infection

Ratio of transmissions from local outbreak and transmissions by travelling donors

Total number of transmissions in the country at risk (or all of Europe if selected)

Total number of transmissions in the country of the outbreak

Calculation:

Maximum risk

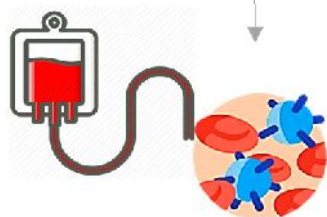
Reset

Add an outbreak/
assessment

EXAMPLE

$$n_i = \sum_j \left(\underbrace{p_{dj} \cdot \varphi_j}_{\text{Donor}} \cdot \underbrace{\frac{f_{v,j,i}}{N_i}}_{\text{Travel}} \right) \cdot \underbrace{D_a (D_a/2 + D_{ia})}_{\text{Risk}}$$

European Travelling donors' risk assessment tool

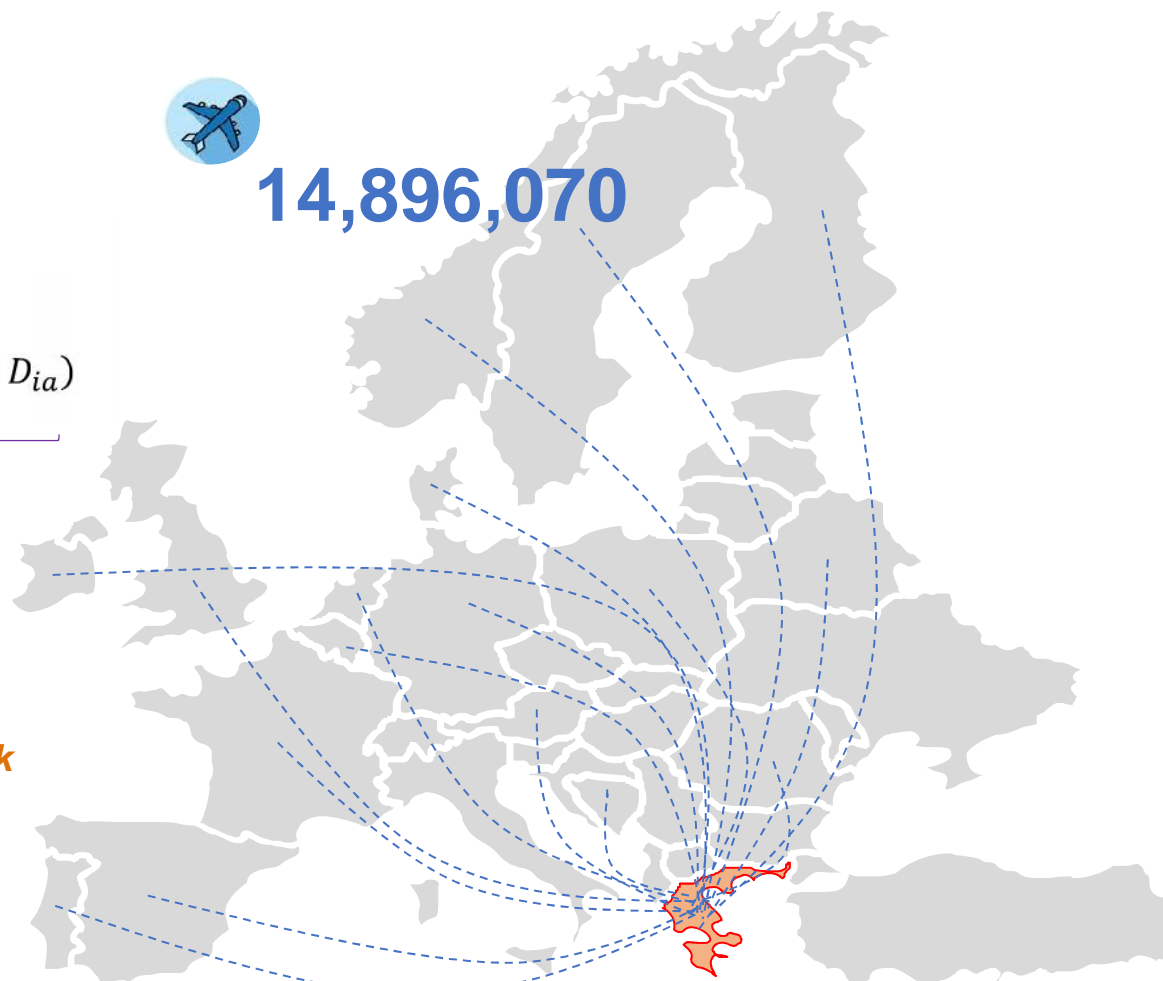


European Travelling donors' risk assessment tool

EUFRAT



14,896,070



2018
234 NI-WNV
human cases

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Calculation:

Maximum risk

Reset

Add an outbreak/
assessment

West Nile Virus
Zika
Chikungunya
West Nile Virus
Other

Click the right arrow
to display the viruses
available

8.0

5.5

Enter the numbers to
change to alternative
values

0.00%

59

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Calculation:

Maximum risk

Reset

Add an outbreak/
assessment

West Nile Virus

▼

Europe
Armenia
Austria
Belgium
Bulgaria
Croatia
Cyprus
Czech Republic

0.00%

Click the right arrow to display the list of available countries.

The name of the country can also be entered manually.

59

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Calculation:	Maximum risk
Reset	Add an outbreak/ assessment

West Nile Virus

Europe

8.0

5.5

▼

- France
- FYR Macedonia
- Georgia
- Germany
- Greece
- Hungary
- Iceland
- Ireland

59

Click the right arrow to display the list of available countries

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Maximum risk

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assessment

West Nile Virus

Europe

8.0

5.5

Greece

234

0.00%

1.53E-04

1.3217

59

2.1E-04

3.27E-05

1.1E-03

34.6

7.7E-03

2.7E-01

Enter the number or cases
reported during the outbreak
in this cell

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Europe

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5.5

Greece

234

99.60%

1.53E-04

1.3217

14,781

2.1E-04

8.18E-03

2.8E-01

34.6

1.9E+00

6.6E+01

Enter the proportion of unobserved and/or asymptomatic cases of infection as a percentage.

Example with NI-cases. Assume 1 NI case for each 250 non-NI cases

Intermediate risk parameters

Intermediate risk parameters – Assessed area

Risk parameters

Country specific travelling donors' risk factor (per day)

1.53E-04



Risk factor associated with characteristics of the blood supply. It considers the number of products distributed in the country of origin and the proportion of donors.

Visitors per inhabitant per year

1.3217



This value shows the number of visitors from the country of origin to the outbreak area per number of inhabitants in the outbreak area per year. **It can be changed**

Disease specific travelling donors' risk factor (days squared)

14,781



This factor indicates the virus specific contribution to the risk of transmission. It considers the duration of the incubation and infectious periods.

Intermediate risk parameter – Outbreak area

Country specific local transmission risk factor (per day)

2.1E-04



This factor is associated with the risk of transmission by donors living in the **outbreak area**. It considers the number of products distributed in the country and the proportion of donors.

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West Nile Virus

Europe

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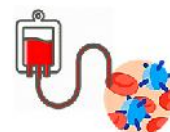
8.18E-03

2.8E-01

34.6

1.9E+00

6.6E+01



1

122 observed infections required for one infected blood product in Europe

4 observed infections required for one infected blood product in Greece

1 required outbreak for one infected blood product in Europe

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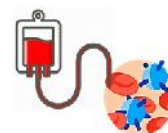
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6.6E+01



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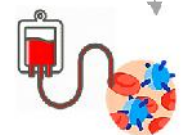
2.8E-01

34.6

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Calculation:

Maximum risk

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assessment

West Nile Virus

$$n_i = \sum_j \left(p_{adj} \cdot \varphi_j \cdot \frac{f_{vj,i}}{N_i} \right) \cdot D_a (D_a/2 + D_{ia})$$

Europe

8.0

5.5

Greece

234

99.60%

1.53E-04

1.3217

14,781

2.1E-04

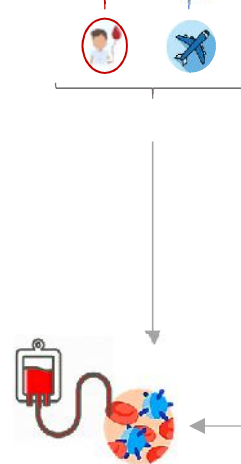
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8.0

5.5

Europe

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1.1442

14,781

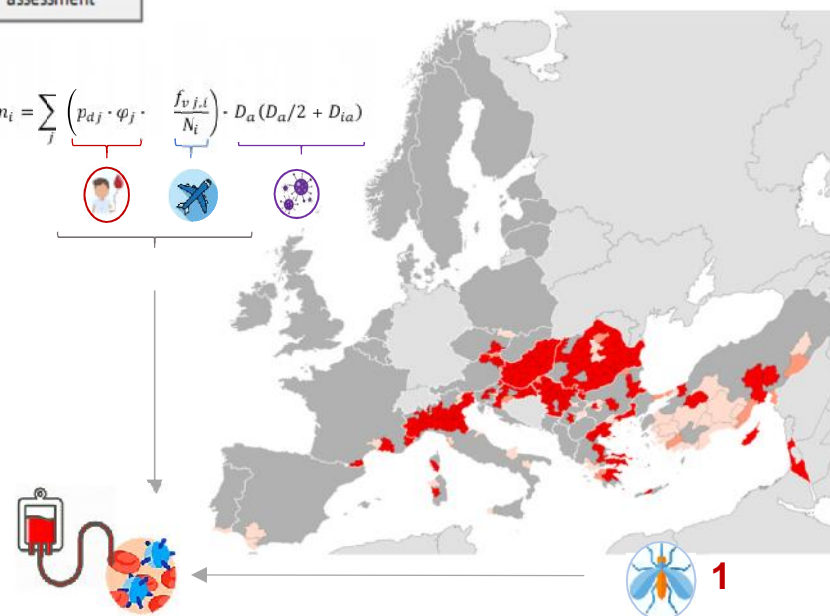
1.6E-04

7.13E-03

2.2E-01

30.5

$$n_i = \sum_j \left(p_{d,j} \cdot \varphi_j \cdot \frac{f_{v,j,i}}{N_i} \right) \cdot D_a (D_a/2 + D_{ia})$$



140 neuroinvasive cases required for one WNV
infected blood product by a **travelling donor**
in Europe

Risk of Infectious Disease Transmission by European Travelling Donors

	Unique outbreak in Greece			General outbreak
	Risk for Greece	Risk for Europe	Ratio	Risk for Europe
Estimated number of transmissions per observed NI infection	0.28	0.0082	34.6	0.0071
Estimated number of NI infections required for one infected blood product	4	122		140
Estimated number of transmissions per observed non-NI infection	0.0057	0.00016	30.5	0.00014
Estimated number of non-NI infections required for one infected blood product	176	6114		7016

Missing data

Estimated number of transmissions by blood products

In the country at risk (or for all of Europe if selected), per observed infection

8.18E-03

122 observed infections required for one infected blood product in Europe

In the country of the outbreak (or for all of Europe if selected), per observed infection

2.8E-01

4 observed infections required for one infected blood product in Greece

Ratio of transmissions from local outbreak and transmissions by travelling donors

34.6

Total number of transmissions in the country at risk (or all of Europe if selected)

8.2E-03

122 required outbreaks for one infected blood product in Europe

Total number of transmissions in the country of the outbreak

2.8E-01

4 required outbreaks for one infected blood product in Greece

3 countries without country specific donor data:

Slovenia

Turkey

Ukraine

For this combination of countries assessed, in 3 countries no data on the blood supply (proportion of donors or number of products distributed) were available and the European averages were applied for these countries

5 countries without travellers data:

Armenia

FYR Macedonia

Georgia

Montenegro

Serbia

For this combination of countries assessed, for 5 countries data regarding travels to the country of the outbreak were not available
Note: These countries were therefore not included in the calculation of the risk

CONCLUSION

- **Risk models** can provide **estimates** based on a limited number of variables only, providing a **framework for blood safety** decision-making.
- The risk of transmission of infections by blood from travelling donors of the arboviruses considered (presuming that these would indeed be transmitted) are comparable in size and **require thousands of infections** to attain **one transfusion transmission**.
- **Local risk of transmission** of the arboviruses considered by blood transfusion are **more than an order of magnitude higher** than the **cumulative risk for the whole European blood supply**, even when this risk is conservatively estimated
- These **risk ratios** provided may **vary per country**, and are most strongly influenced by the nations **travelling habits**

Thank you!



European Travelling donors' risk assessment

(Grey cells are input fields)

Virus assessed

Select virus to assess (or select other)

Calculation:

Maximum risk

Reset

Add an outbreak/
assessment

West Nile Virus

Country assessed

Select country or region at risk to evaluate

Europe

Disease characteristics

Duration of latent period of acute infection (days)

8.0

Duration of infectious period during the acute phase of the disease (days)

5.5

Outbreak characteristics

European country of outbreak

Europe

Number of observed infections

1339

Proportion of unobserved/ asymptomatic infections

99.60%

Risk parameters

Country specific travelling donors' risk factor (per day)

1.54E-04

Visitors per inhabitant per year

1.1442

Disease specific travelling donors' risk factor (days squared)

14,781

Country specific local transmission risk factor (per day)

1.6E-04

Estimated number of transmissions by blood products

In the country at risk (or for all of Europe if selected), per observed infection

7.13E-03

In the country of the outbreak (or for all of Europe if selected), per observed infection

2.2E-01

Ratio of transmissions from local outbreak and transmissions by travelling donors

30.5

Total number of transmissions in the country at risk (or all of Europe if selected)

9.5E+00

Total number of transmissions in the country of the outbreak

2.9E+02

140 observed infections required for one infected blood product in Europe

5 observed infections required for one infected blood product in Europe

0 required outbreak for one infected blood product in Europe

0 required outbreak for one infected blood product in Europe