VECTOR-BORNE DISEASES AND BLOOD SAFETY: A EUROPEAN PERSPECTIVE

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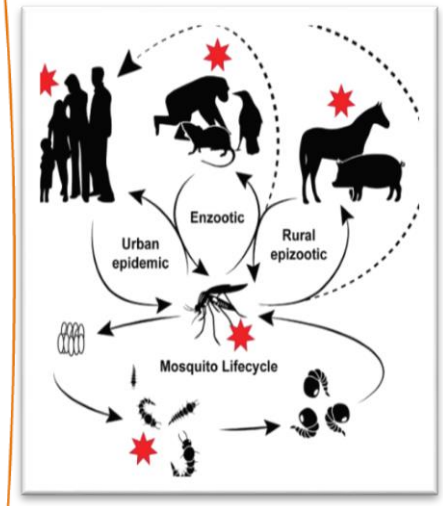
- Conclusions

ARBOVIRAL (arthropod-borne viral) INFECTIONS



Encephalitis, meningitis, Gillian-Barré Syndrome.

MTC complications (1-13%) ZIKV

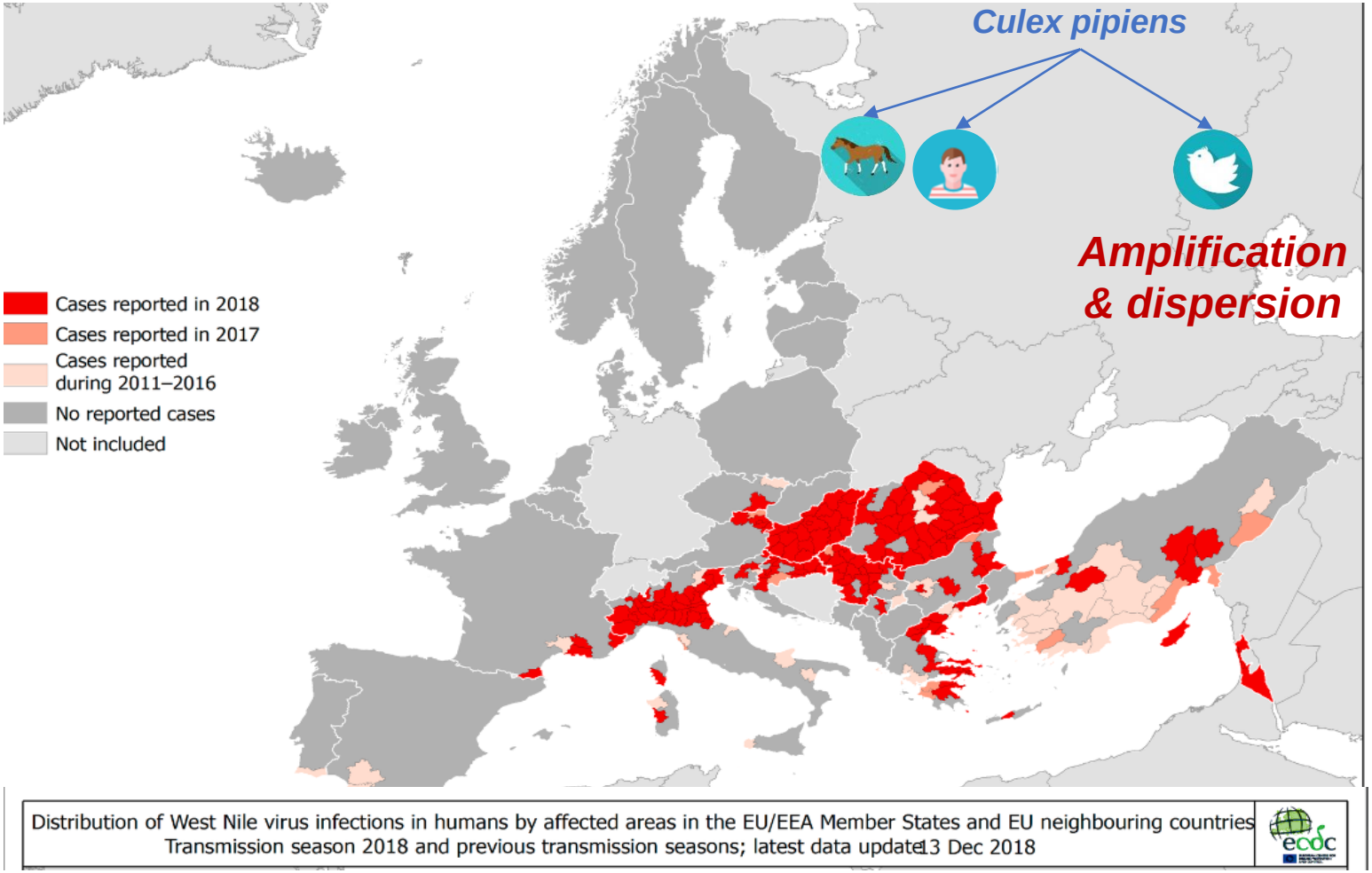
Death. Mainly among elderly and comorbidities or coinfections

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



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

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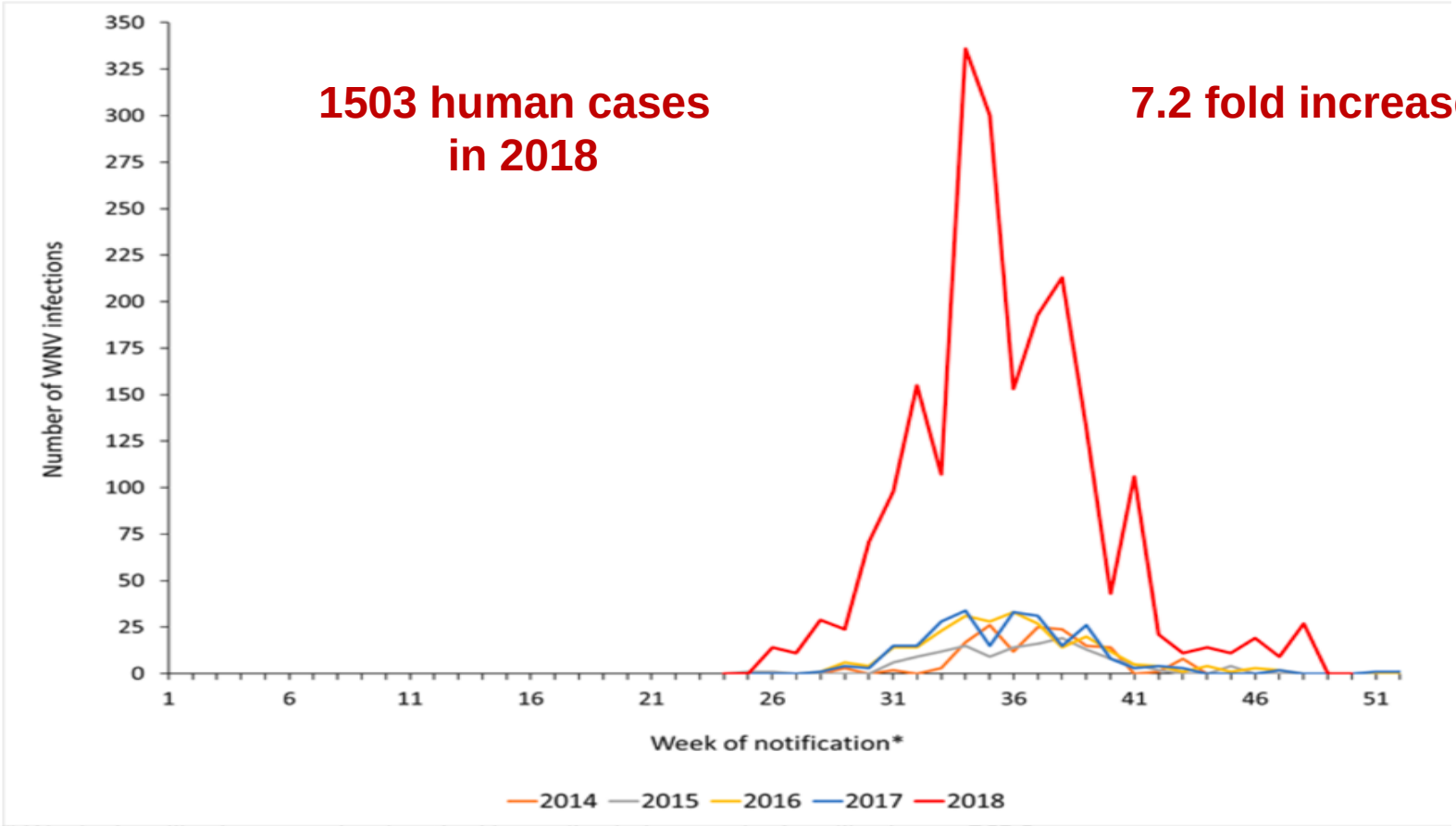
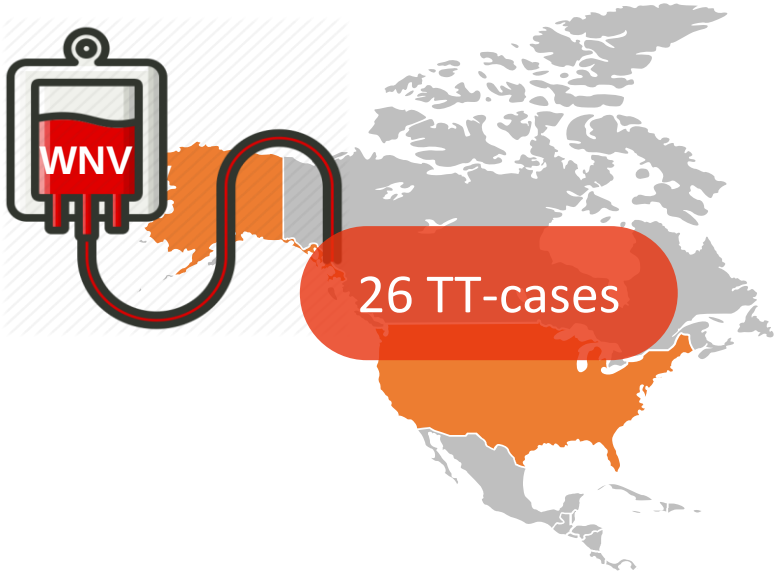
Number of WNV infections in EU/EEA and EU enlargement countries by epidemiological week of notification*, 2014-2018.



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

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**?

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OBJECTIVES

1) Estimate the **risk of emerging infection transmission throughout Europe**

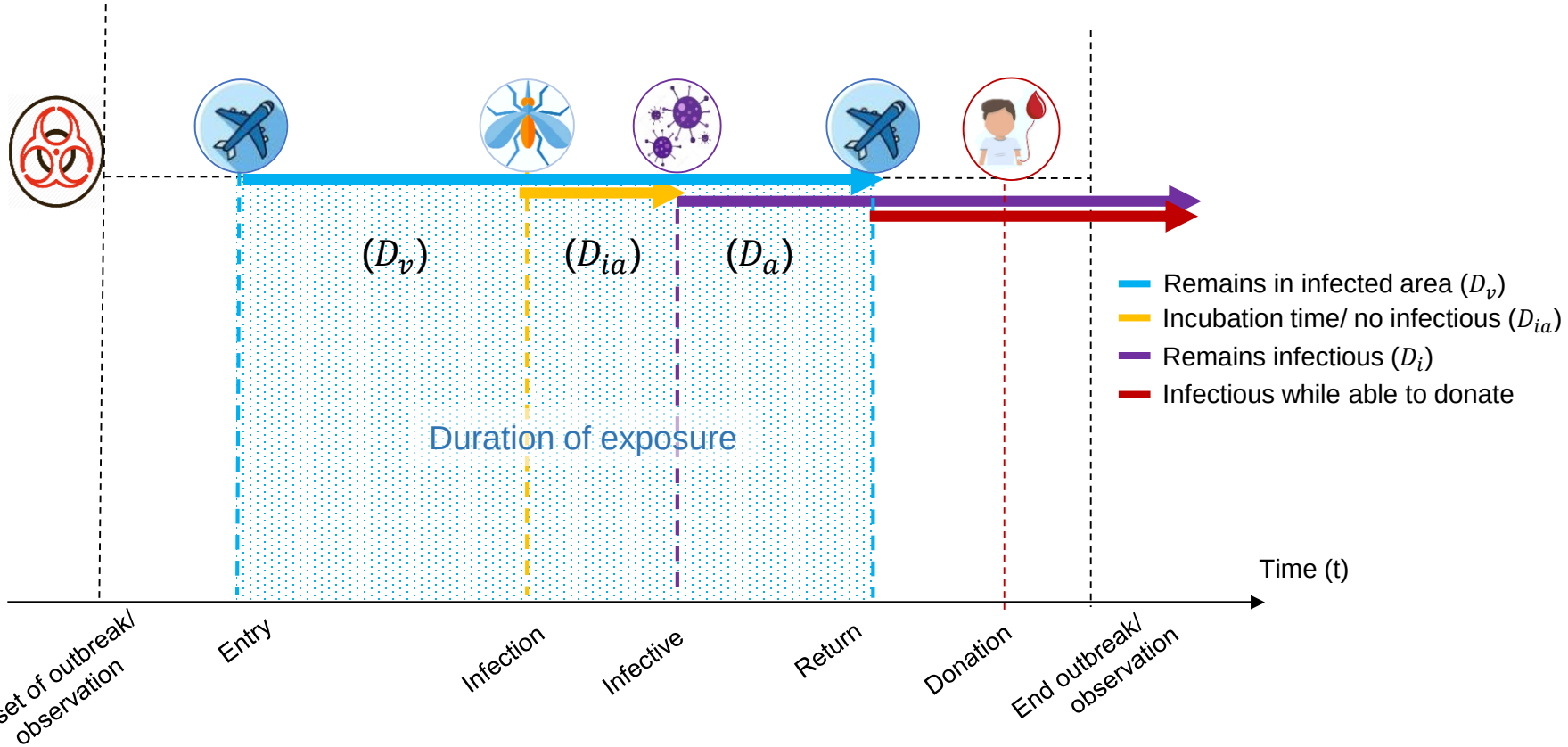
2) Develop a **simple tool** to calculate the **combined risk of disease transmission** for outbreaks in specific countries/areas for **Europe as a whole**

3) Derive the number of **infections transmitted by blood transfusion throughout Europe** per observed infection in Europe (R_{0t})

4) Generate an easy way to estimate 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.



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

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

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

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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

COUNCIL OF EUROPE
CONSEIL DE L'EUROPE
eurostat
NCBI PubMed

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 Blood Alliance

- European Travelling donors´ risk assessment tool -

European Travelling donors' risk assessment

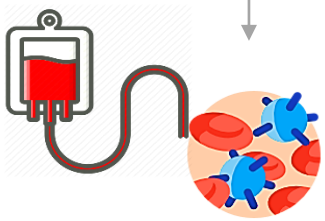
(Grey cells are input fields)

Calculation:	Maximum risk
Reset	Add an outbreak/ assessment
Virus assessed	
Select virus to assess (or select other)	
Country assesed	
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	0.00%
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	

EXAMPLE

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

European Travelling donors´ risk assessment tool



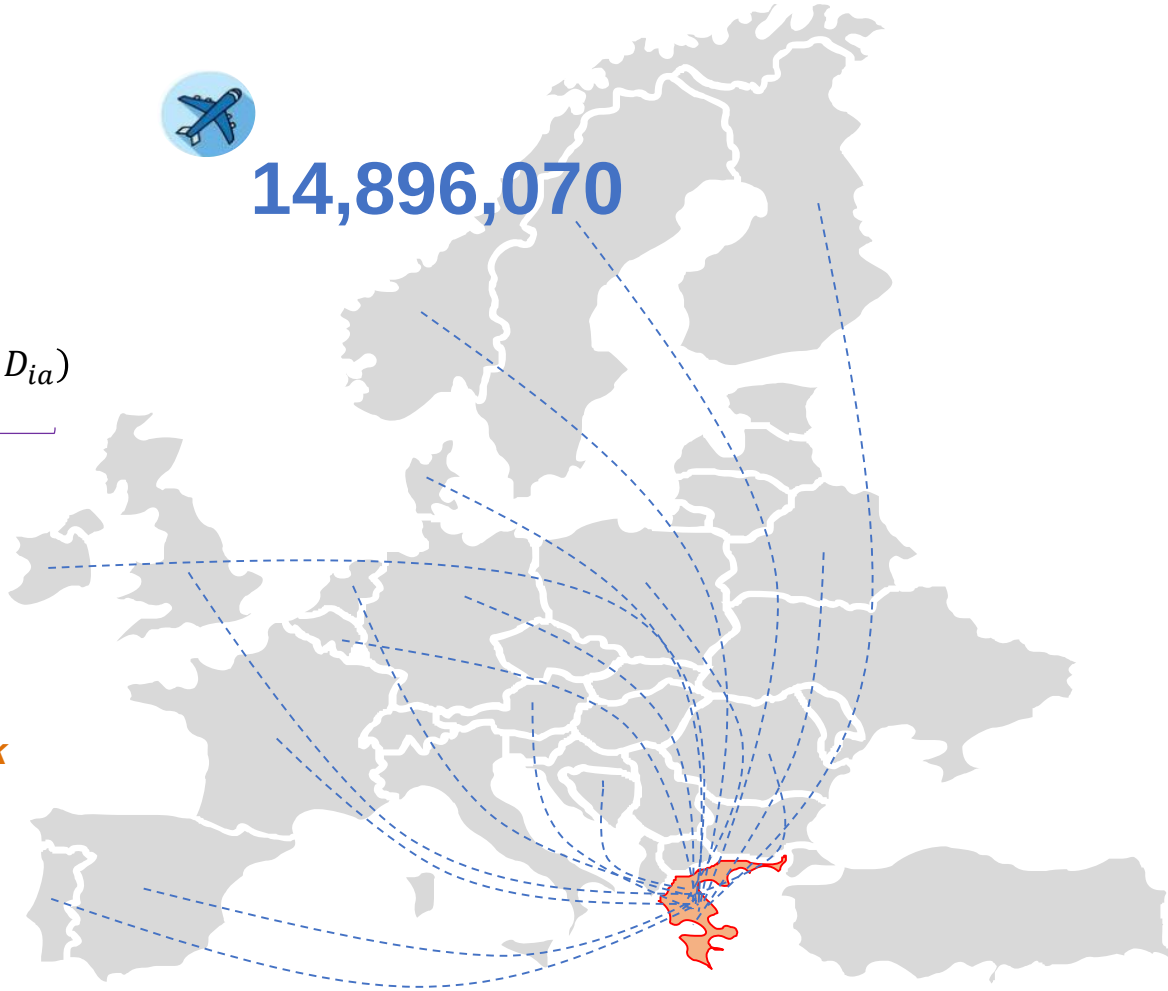
European Travelling donors´ risk assessment tool

EUFRAT

2018

234 NI-WNV human cases

14,896,070



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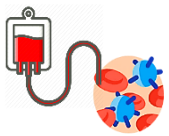
European Travelling donors' risk assessment

(Grey cells are input fields)

Calculation:	Maximum risk
Reset	Add an outbreak/ assessment

Virus assessed	
Select virus to assess (or select other)	West Nile Virus
Country assesed	
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	Greece
Number of observed infections	234
Proportion of unobserved/ asymptomatic infections	99.60%
Risk parameters	
Country specific travelling donors' risk factor (per day)	1.53E-04
Visitors per inhabitant per year	1.3217
Disease specific travelling donors' risk factor (days squared)	14,781
Country specific local transmission risk factor (per day)	2.1E-04



1

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)	1.9E+00	1 required outbreak for one infected blood product in Europe
Total number of transmissions in the country of the outbreak	6.6E+01	0 required outbreak for one infected blood product in Greece

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European Travelling donors' risk assessment

(Grey cells are input fields)

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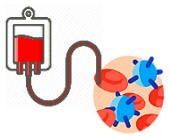

234

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

0 required outbreak for one infected blood product in Greece

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European Travelling donors' risk assessment

(Grey cells are input fields)

Calculation:	Maximum risk	
Reset	Add an outbreak/ assessment	

Virus assessed

Select virus to assess (or select other)	West Nile Virus

Country assesed

Select country or region at risk to evaluate	Europe

Disease characteristics

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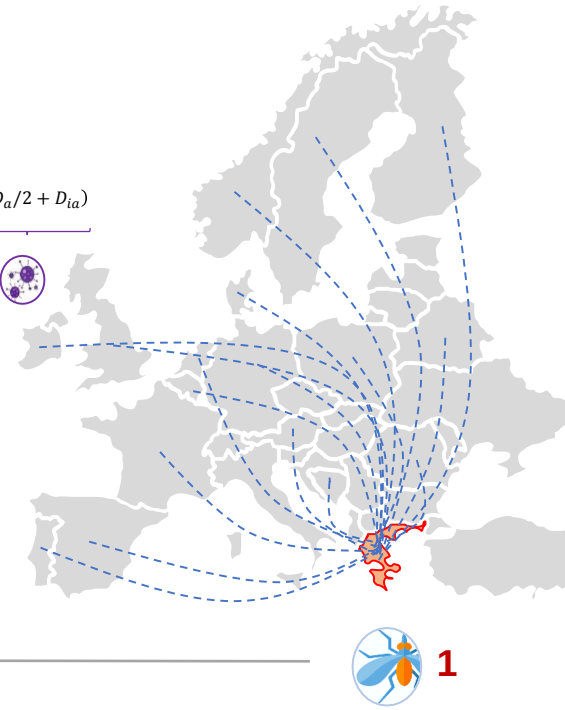
$$n_i = \sum_j \left(p_{dj} \cdot \varphi_j \cdot \frac{f_{v\,j,i}}{N_i} \right) \cdot D_a \left(D_a/2 + D_{ia} \right)$$



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European Travelling donors' risk assessment

(Grey cells are input fields)

Calculation:	Maximum risk	
Reset	Add an outbreak/ assessment	

Virus assessed

Select virus to assess (or select other)	West Nile Virus

Country assesed

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	Greece
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Risk parameters

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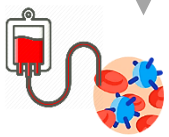

234

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
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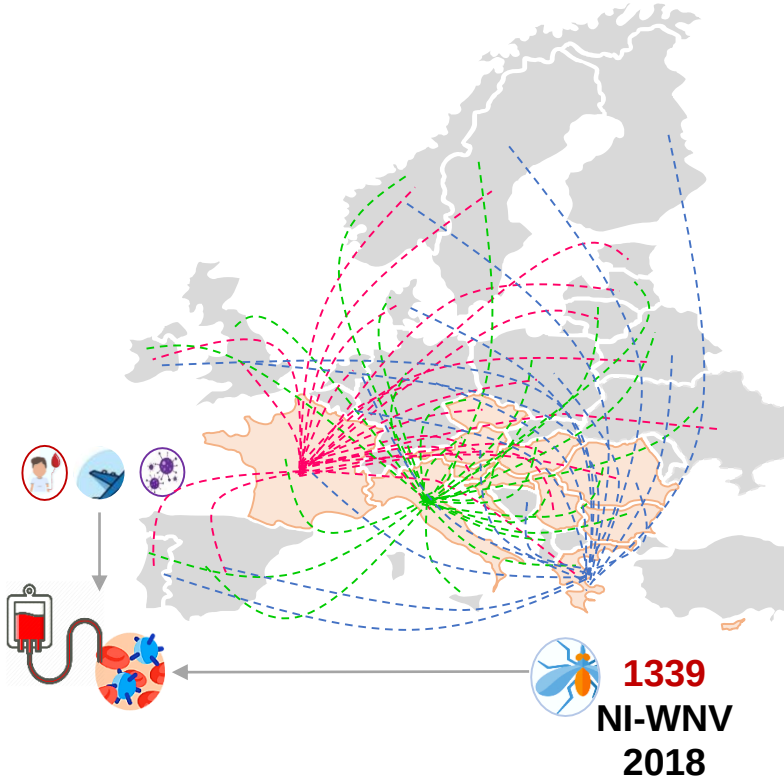
European Travelling donors' risk assessment

Grey cells are input fields

		Maximum risk	
	Reset	Add an outbreak/ assessment	
Virus assessed			
Select virus to assess (or select other)	West Nile Virus	West Nile Virus	West Nile Virus
Country assesed			
Select country or region at risk to evaluate	Europe	Europe	Europe
Disease characteristics			
Duration of latent period of acute infection **(Dia)**	8.0	8.0	8.0
Duration of infectious period during the acute phase of the disease **(Da)**	5.5	5.5	5.5
Outbreak characteristics			
European country of outbreak	France	Greece	Italy
Number of observed infections	7	234	234
Proportion of unobserved/ asymptomatic infections	99.60%	99.60%	99.6%
Risk parameters			
Country specific travelling donors' risk factor	1.45E-04	1.53E-04	1.57E-04
Visitors per inhabitant per year	0.5309	1.3217	0.6821
Disease specific travelling donors' risk factor	14,781	14,781	14,781
Country specific local transmission risk factor	1.6E-04	2.1E-04	1.6E-04
Estimated number of transmissions by blood products			
In the country at risk (or all of Europe if selected) per observed infection	3.1E-03	8.2E-03	4.3E-03
In the country of the outbreak (or all of Europe if selected), per observed infection	2.2E-01	2.8E-01	2.2E-01
Transmissions from local outbreak divided by transmissions by travelling donors	70.9	34.6	51.7

				Total
Total number of transmissions in the country of origin (or all of Europe if selected)	2.2E-02	1.9E+00	1.0E+00	4.78E+00
Total number of transmissions in the country of the outbreak	1.55E+00	6.63E+01	5.25E+01	3.56E+02



1339 NI-WNV 2018

Based on the **1339** human neuro-invasive cases of WNV infections reported in Europe during 2018 the **estimated number of blood products with WNV** (given that no safety interventions would be in place) **is 4.78**

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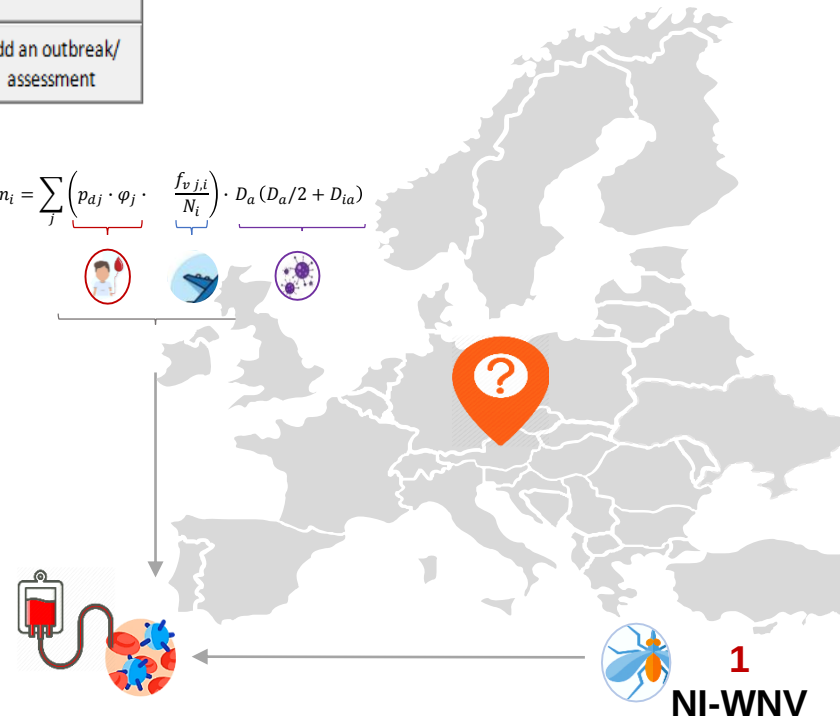
European Travelling donors' risk assessment

(Grey cells are input fields)

Calculation:	Maximum risk
Reset	Add an outbreak/ assessment

Virus assessed	
Select virus to assess (or select other)	West Nile Virus
Country assesed	
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	1
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

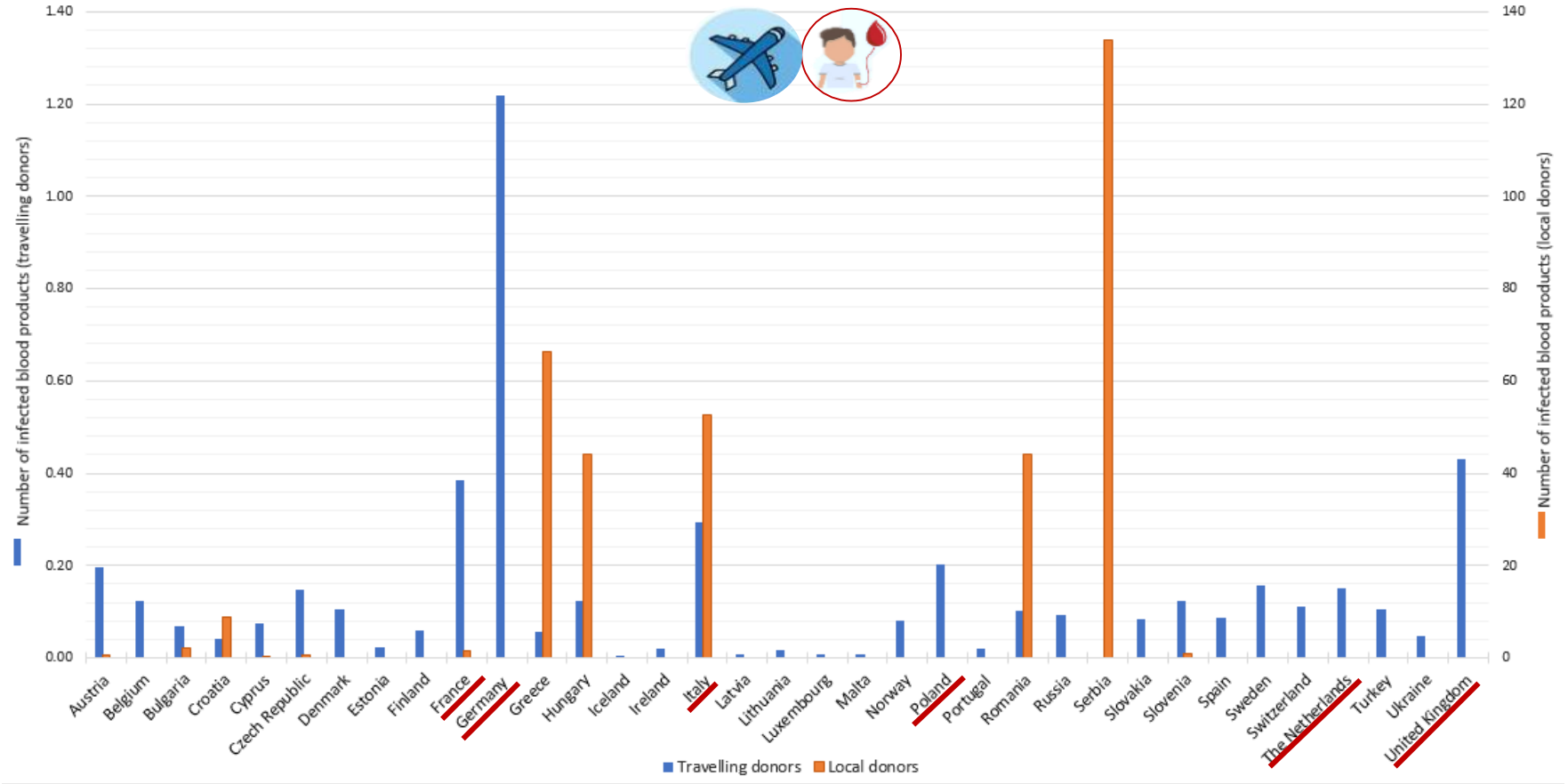
$$n_i = \sum_j \left(p_{dj} \cdot \varphi_j \cdot \frac{f_{v\,j,i}}{N_i} \right) \cdot D_a \left(D_a/2 + D_{ia} \right)$$



140 observed infections required for one infected blood product in Europe

5 observed infections required for one infected blood product in Europe

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



Given the characteristics of the European blood supplies and travels within Europe, in order to have **one infected blood product** of **WNV in Europe** would be necessary on average **7016 observed WNV infections**, or **140 neuro-invasive cases** of WNV infection

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Risk of Infectious Disease Transmission by European Travelling Donors

	Unique outbreak in Greece		Multiple outbreaks	Outbreak in Europe
	Risk for Greece	Risk for Europe	Risk for Europe	Risk for Europe
Estimated number of transmissions per observed **NI infection**	0.28	0.0082	0.0036	0.0071
Estimated number of **NI infections** required for one infected blood product	4	122	279	140
Estimated number of transmissions per observed **non-NI infection**	0.0057	0.00016	0.000071	0.00014
Estimated number of **non-NI infections** required for one infected blood product	176	6114	13992	7016

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**

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Thank you!