Valuing
the risk of emerging
infectious diseases for blood
transfusion safety

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Malta, 7th October 2015

University Medical Center
Utrecht

Who we are and what we do

- **_Transfusion Technology Assessment_** department is a collaboration between the Dutch blood transfusion operator and the Julius Center for Health Sciences and Primary Care

- Assignment: to developing quantitative models for decision support.

- Studies we do:

  - Cost-effectiveness of safety interventions

  - Risk of infection transmission by emerging infectious diseases

  - Modelling haemophilia patient treatment strategies with plasma derived medicines

  - Modelling donor / recipient population (dynamics)

  - Decision support for unacceptable number of infections per center

  - Collect and analyse transfusion data for the EU

Blood safety and decision making

Complicating factors are related to:

1. the (risk) assessments

   - Blood is a complex biological material
   - Every human is unique

2. the decision making processes

   - Different products, different (national and international) regulations and contexts
   - Different stakeholders / perspectives

3. the setting

   - Public sensitive
   - Expensive (Sanquin turnover 430 mln Euro per year)
   - Continuously changing

Blood transfusion chain in a nutshell
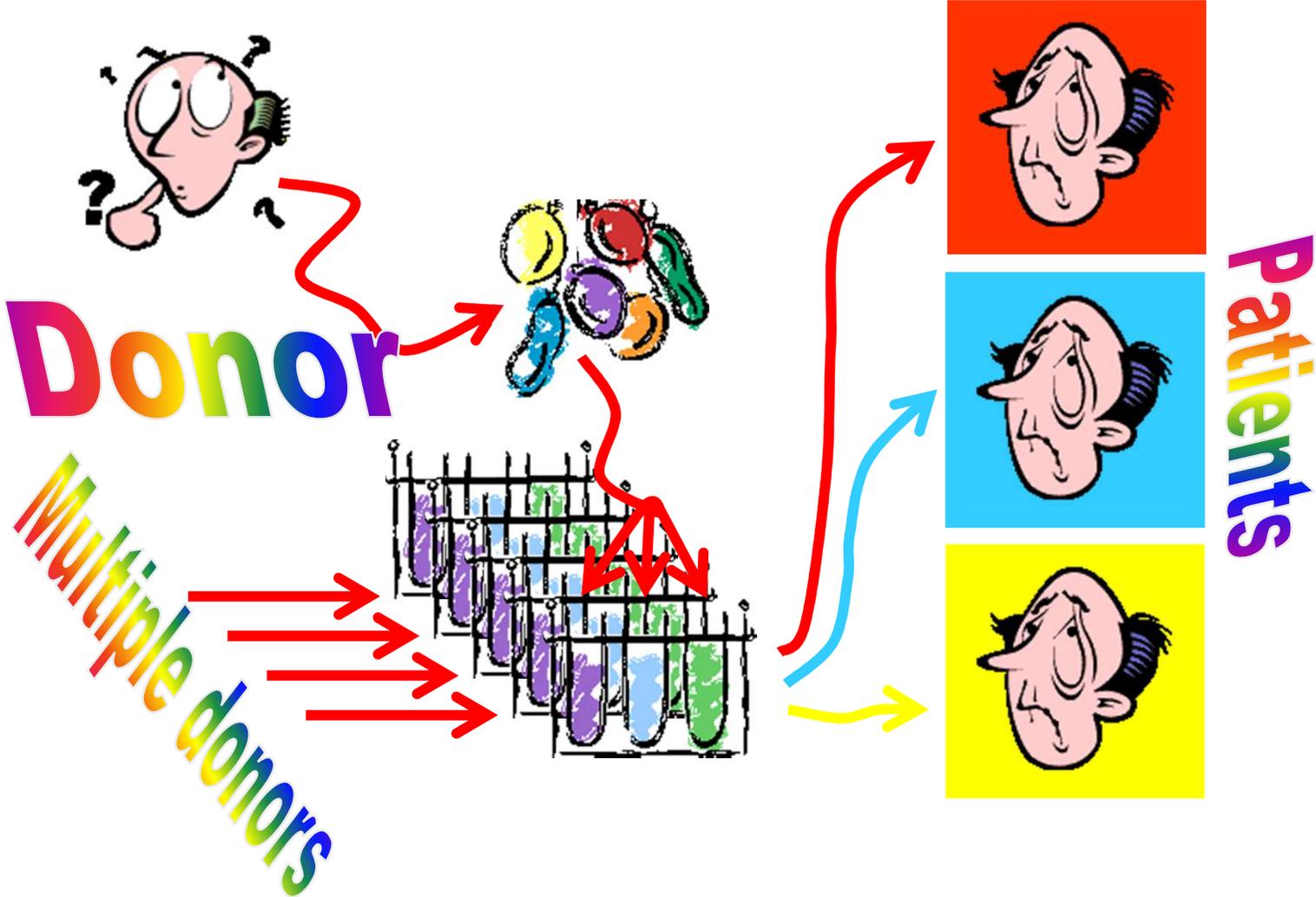
Blood transfusion chain in a nutshell

RBCs:
1 → 1

PLTs:
5 → 1

Plasma:
1 → 1
Medicines:
10 000 →
1000
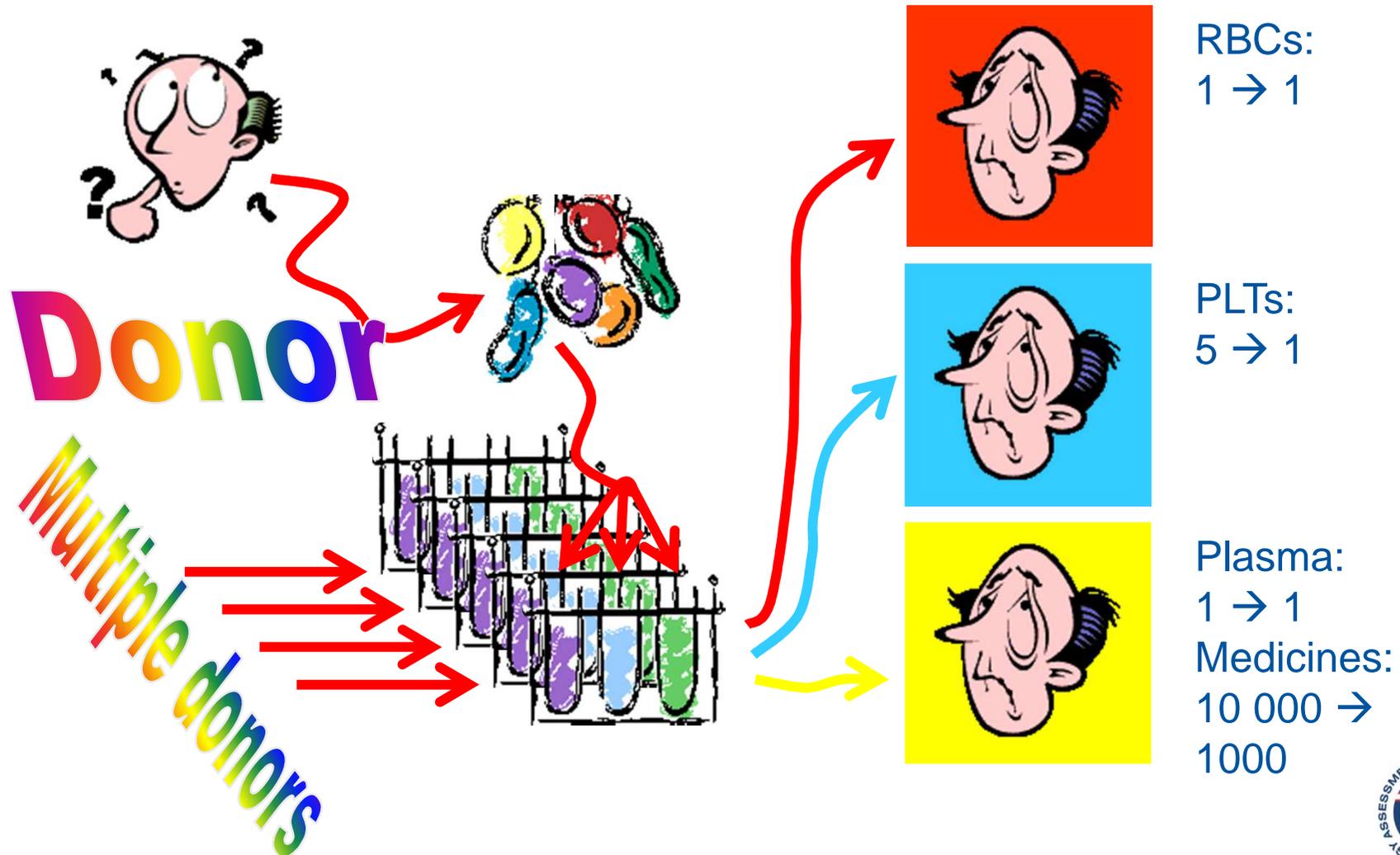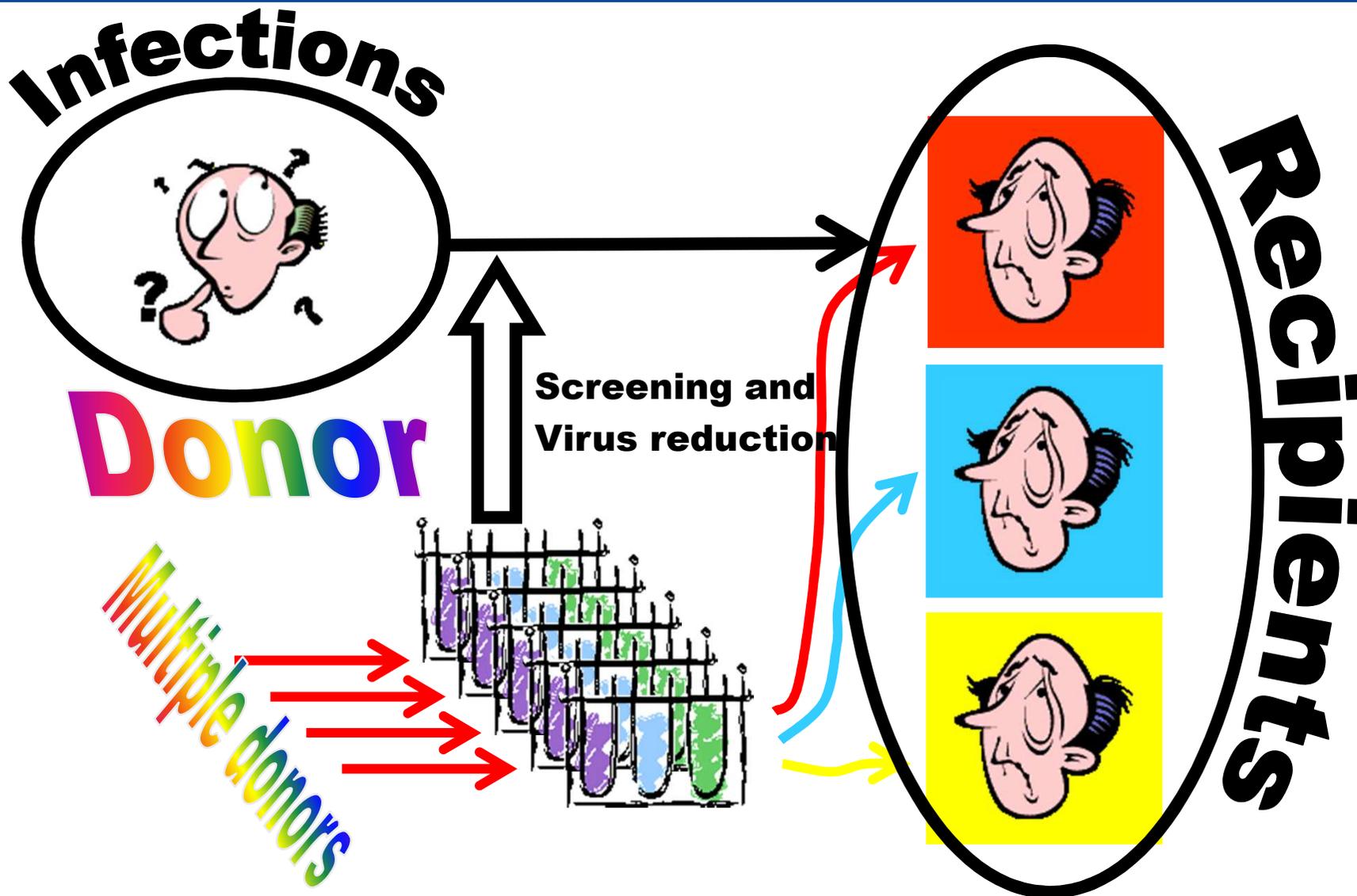
A science that evolved over time…

A "Dead serious" topic

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Prison sentences for French blood transfusion officials

> 31 October 1992
> Magazine issue 1845. **Subscribe and save**

Three former French health officials were convicted last week by a Paris court on charges of fraud, for allowing HIV-contaminated blood products to be given to haemophiliacs in 1985.

By delaying the introduction of heat treatment to destroy the virus, they exposed thousands of people to contaminated blood products. Some 1500 haemophiliacs were infected with HIV and at least 256 have since died of AIDS (This Week, 15 August).

A "Dead serious" topic

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Prison sentences for French blood transfusion officials

) 31 October 1992

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Anger over French blood trial

Wednesday, November 4, 1992 - 11:00

Anger over French blood trial

By Catherine Brown

French haemophiliac groups, relatives of the victims and ACT UP, the anti-AIDS action group, have denounced as inadequate the sentence of three state-employed doctors, who have been convicted of knowingly allowing the distribution of HIV-contaminated blood that resulted in the death of more than 250 people.

A "Dead serious" topic

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Tuesday, March 9, 1999 Published at 11:03 GMT

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Blood scandal ministers walk free

Cleared: Georgina Dufoix and former boss Laurent Fabius

Former French Premier Laurent Fabius and one of his ex-ministers have been acquitted of manslaughter in France's tainted blood scandal.

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Relevant Stories

26 Feb 99 | Europe
French Aids trial ends

09 Feb 99 | Medical notes
Blood: The risks of infection

27 Nov 98 | Aids
Aids drugs factfile

Internet Links

UNAIDS

Abbott Laboratories

French haemophiliac groups, relatives of the victims and ACT UP, the anti-AIDS action group, have denounced as inadequate the sentence of three state-employed doctors, who have been convicted of knowingly allowing the distribution of HIV-contaminated blood that resulted in the death of more than 250 people.

A "Dead serious" topic

Table 2. Individuals Criminally Indicted for Blood-Supply Safety Concerns

| Country	Persons Charged	Affiliation	Charge	Year of Indictment	Court Decision
France	Michel Garretta	Former head, National Blood Transfusion Center	Poisoning in 1983–1985	1991	Convicted in 1992
	Jean-Pierre Allain	Former research chief, National Blood Transfusion Center	Poisoning in 1983–1985	1991	Convicted in 1992
	Jacques Roux	Former director general, Health Ministry	Poisoning in 1983–1985	1991	Convicted in 1992
	Robert Netter	Former director, National Health Laboratory	Poisoning in 1983–1985	1991	Acquitted in 1992
	Laurent Fabius	Former Prime Minister	Manslaughter in 1983–1985	1994 and 1998	Acquitted in 1999
	Edmond Hervé	Former Secretary of State for Health	Manslaughter in 1983–1985	1994 and 1998	Convicted in 1999; was never sentenced
	Georgina Dufoix	Former Minister of Social Affairs	Manslaughter in 1983–1985	1994 and 1998	Acquitted in 1999
Germany	Director and four staff members	UB Plasma Corp.	Inflicting bodily harm in 1987–1993	1994	Convicted in 1995
	Frank Giesbert and Günter Eckert	Haemoplas Corp.	Murder in 1986 and 1987	1995	Convicted in 1997
Switzerland	Alfred Haessig	Former director, Swiss Red Cross	Endangering the safety of patients with hemophilia in 1985 and 1986	1995	Convicted in 1998; received a 1-year suspended sentence
Japan	Takeshi Abe	Former head, government AIDS study group and chairman, internal medicine department of Teikyo University, Tokyo	Professional negligence leading to death in 1983–1988	1996	Acquitted in 2001
	Takehiko Kawano	President, Green Cross Corp.	Professional negligence leading to death in 1986–1988	1996	Convicted in 2000; sentenced to prison
	Renzo Matsushita	Former President, Green Cross Corp.	Professional negligence leading to death in 1986–1988	1996	Convicted in 2000; sentenced to prison
	Tadakazu Suyama	Former President, Green Cross Corp.	Professional negligence leading to death in 1986–1988	1996	Convicted in 2000; sentenced to prison
	Akihito Matsumura	Former official, Ministry of Health and Welfare	Knowingly perpetuating the spread of HIV infection through the blood supply in 1986–1988	1996	Convicted in 2000; received a 1-year suspended sentence

Legal, Financial, and Public Health Consequences of HIV Contamination of Blood and Blood Products in the 1980s and 1990s
Weinberg PD, Hounshell J, Sherman LA, *Et al*. Ann Intern Med. 2002;136:312-319.

Julius Center.nl Health Sciences and Primary Care

Geographic origins of EID events (1940 - 2004)

Reference: K. Taylor et al. Global Trends in Emerging Infectious Diseases. Nature 2008; 451: 990-993

Julius Center.nl Health Sciences and Primary Care
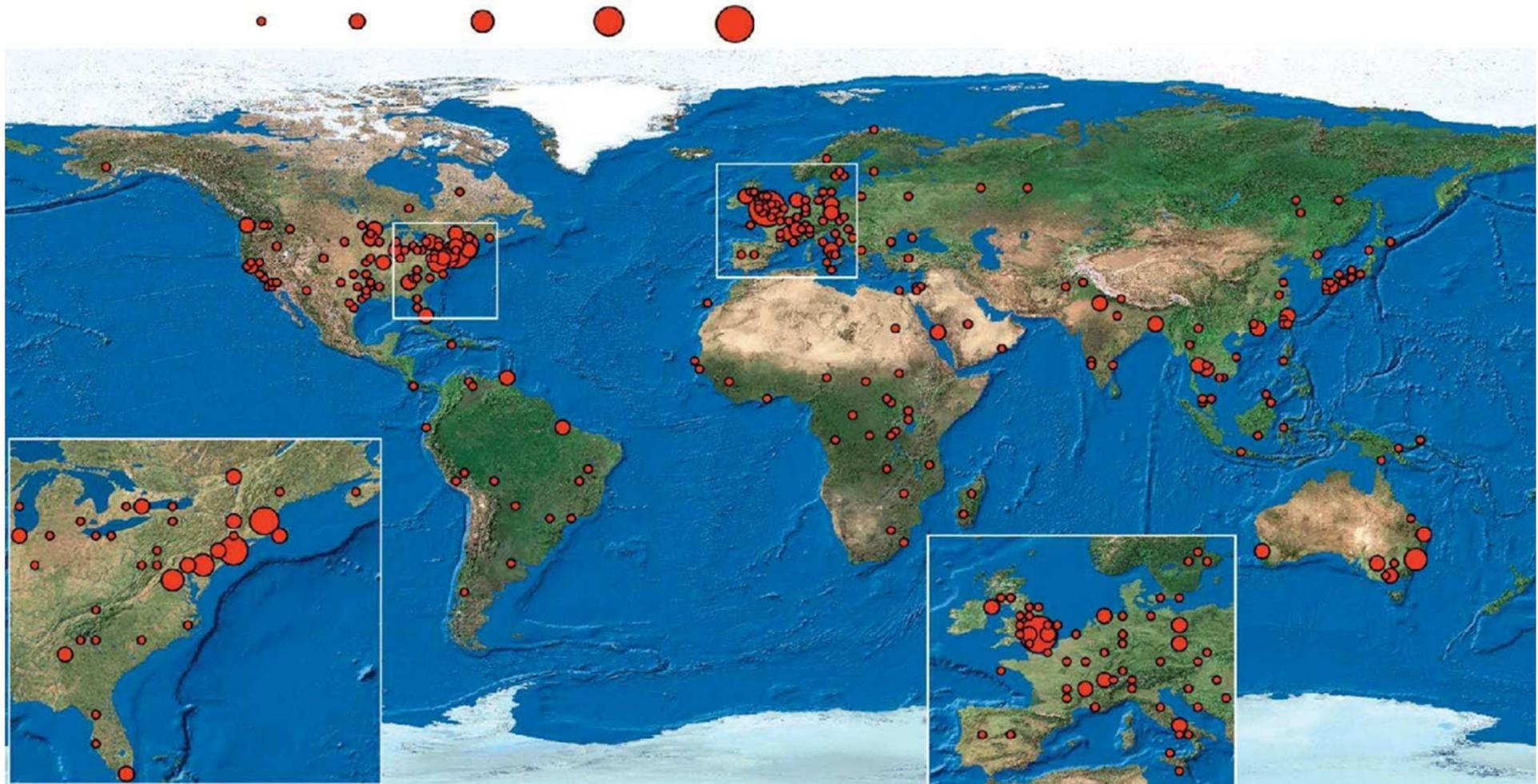
Q-fever in the Netherlands

Details on the epidemic

2007 — Notified Q fever patients, N=196. Source: RIVM Epidemiology & Surveillance

2008 — Gemelde Q-koorts patiënten 2008 01-01-08 t/m 03-12-2008, per 3-cijferig postcodegebied, N = 998*. Bron: RIVM/ EPI

2009 — Gemelde Q-koortspatiënten 2009
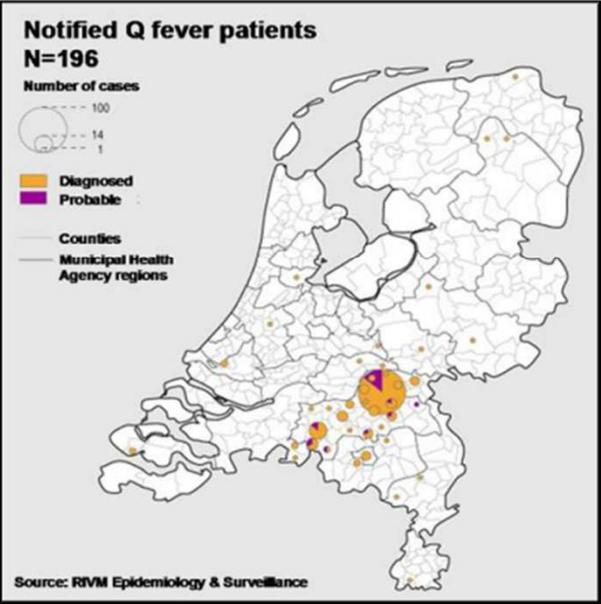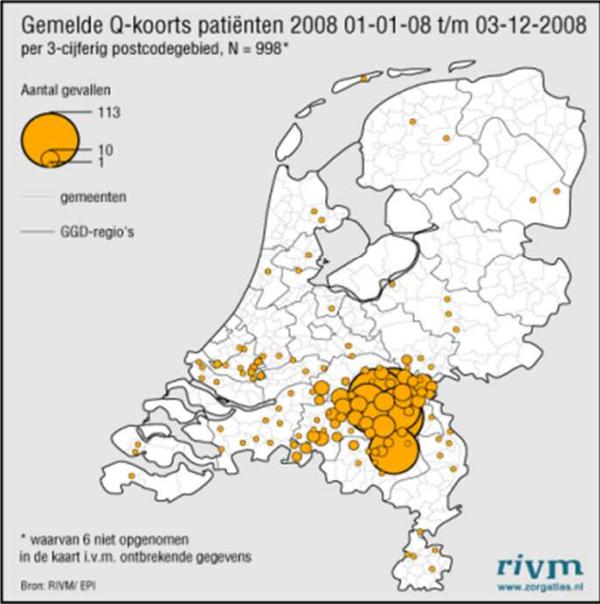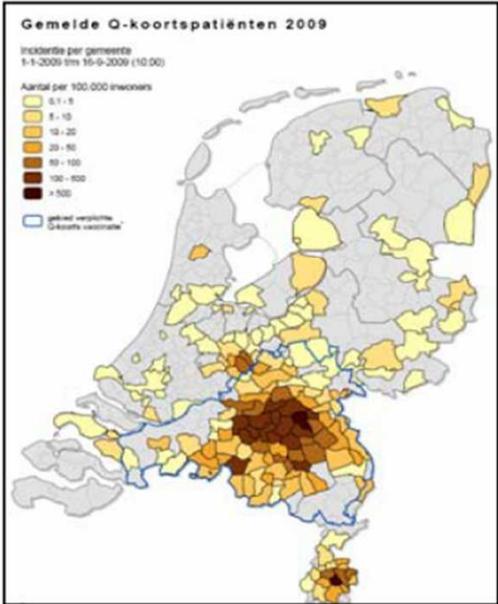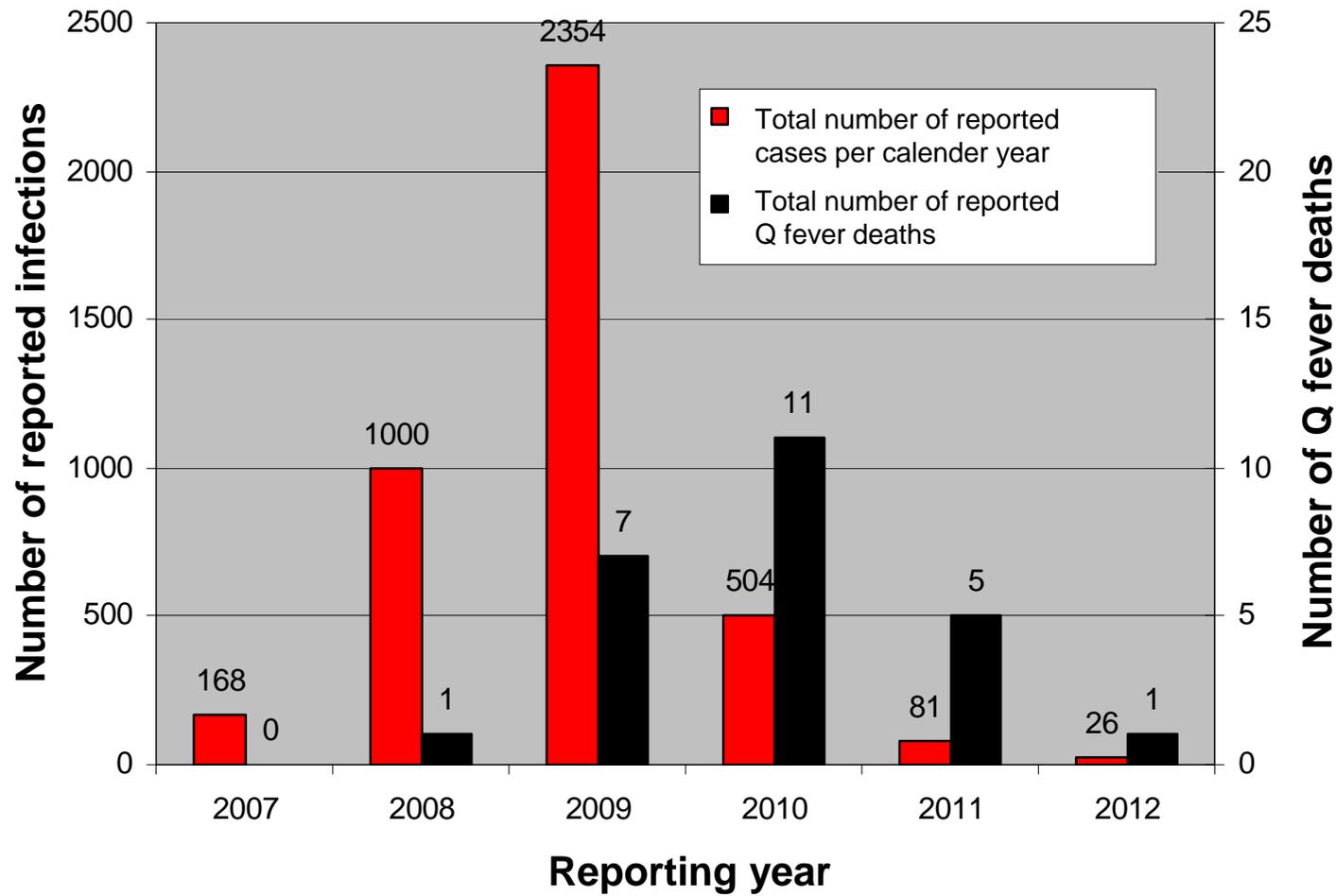
Climate change and climate conditions for Chikungunya transmission
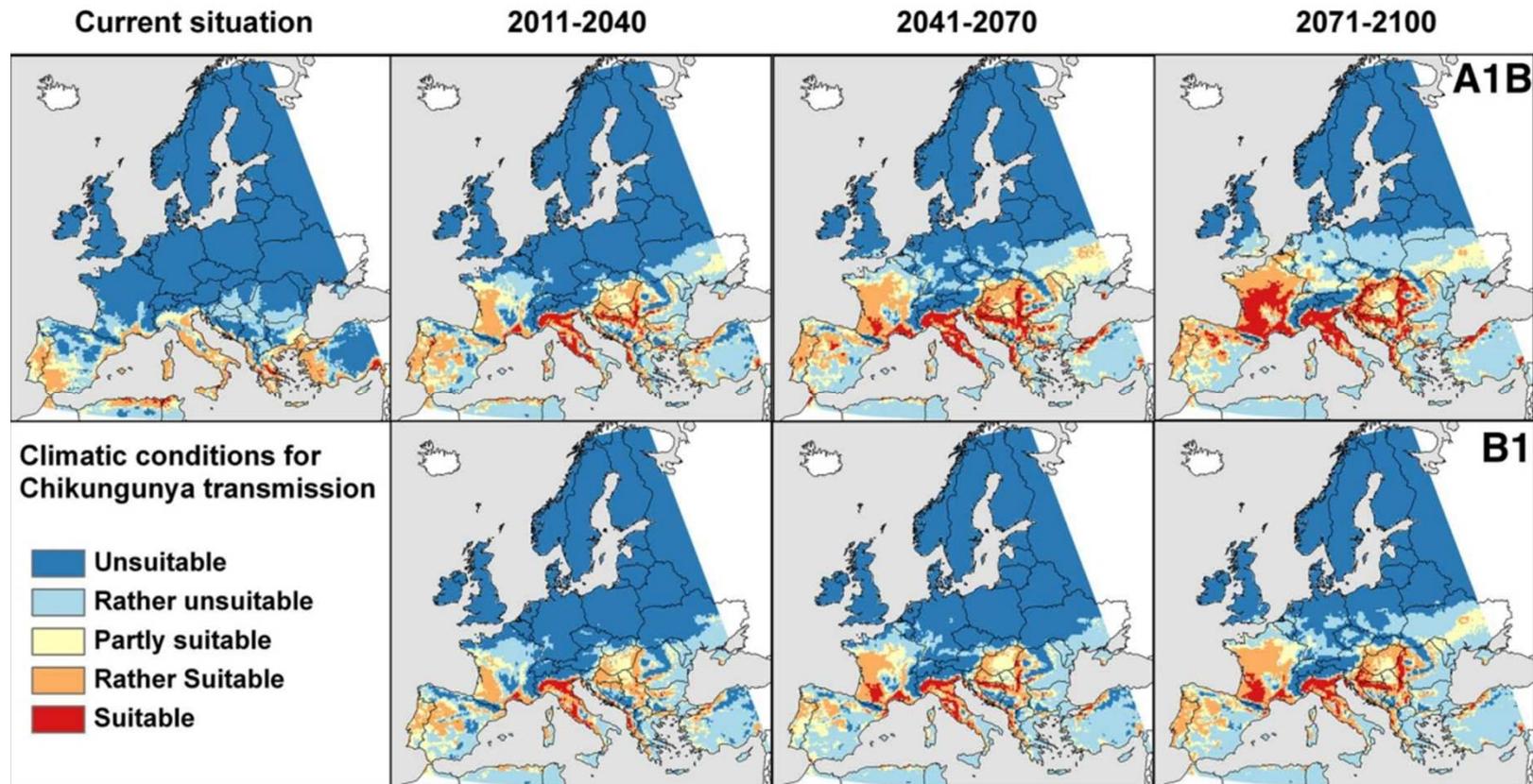
Risk map for Chikungunya transmission in Europe generated by combining temperature requirements of the Chikungunya virus with the climatic suitability of the vector *Aedes albopictus*. Projections for different time-frames are based on two emission scenarios (A1B and B1) from the Intergovernmental Panel on Climate Change, implemented in the regional climate model COSMO-CLM.

Reference: Fischer et al, International Journal of Health Geographics, 2013, Vol. 12:51.

West Nile Virus cases in/around Europe

Distribution of West Nile fever cases by affected areas, European region and Mediterranean basin
Transmission season 2015; latest data update 10 Sep 2015

One or more reported cases
No reported cases
Not included

ECDC. Map produced on: 11 Sep 2015
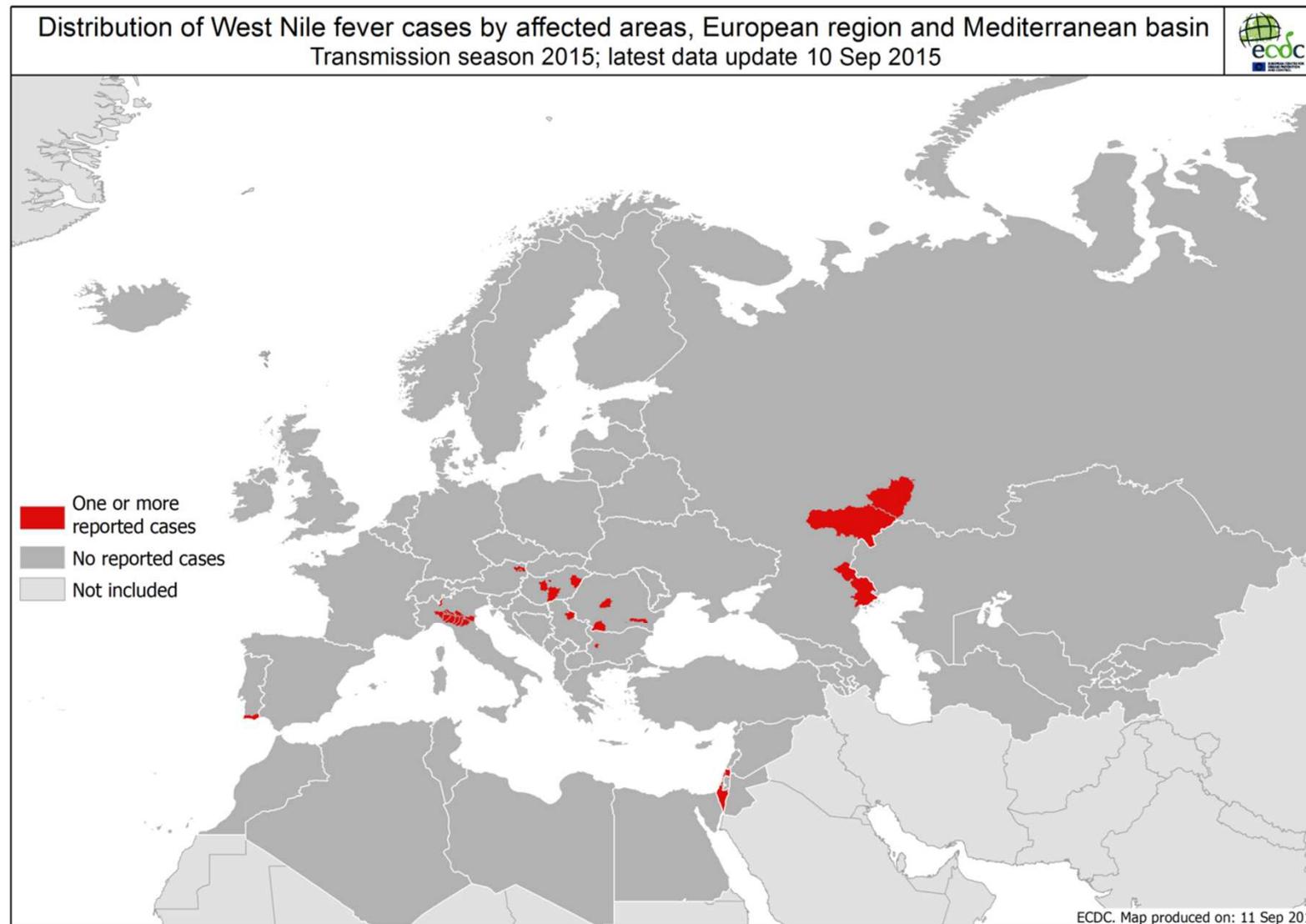
Other newcomers

Leishmaniasis

U. Ehehalt et al.

A) Cutaneous leishmaniasis
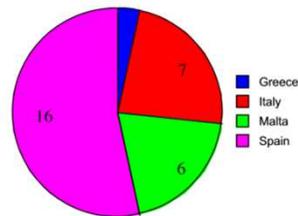
B) Visceral leishmaniasis
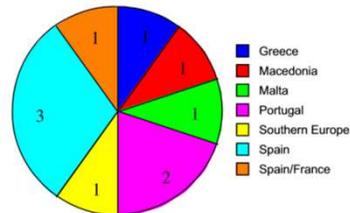
C) Countries of residence
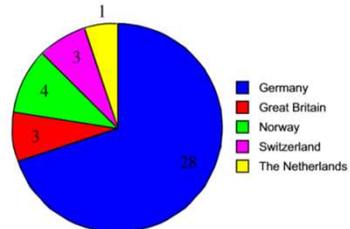
Figure 1 Countries in which leishmaniasis was acquired, separated by cutaneous (CL) and visceral leishmaniasis (VL), and countries of origin of infected tourists.

Trypanosoma cruzi (Chagas disease)
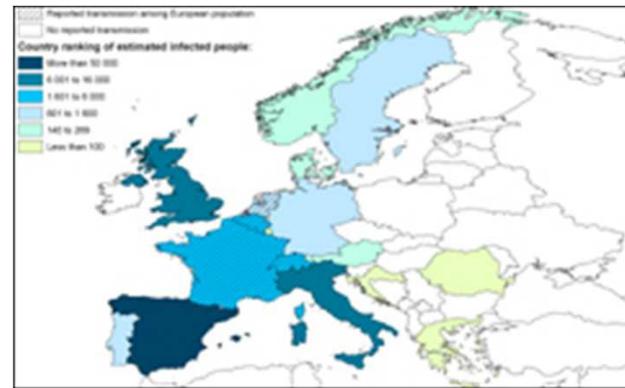
Babesiosis transmitting Ticks

Ixodes ricinus
Current known distribution: July 2015

- Present
- Antic. Absent
- Obs. Absent
- No data
- Unknown

Outermost regions
- Azores (PT)
- Canary Islands (ES)
- Madeira (PT)
- Svalbard/Jan Mayen (NO)

ECDC-EFSA 2015/VECTORNET
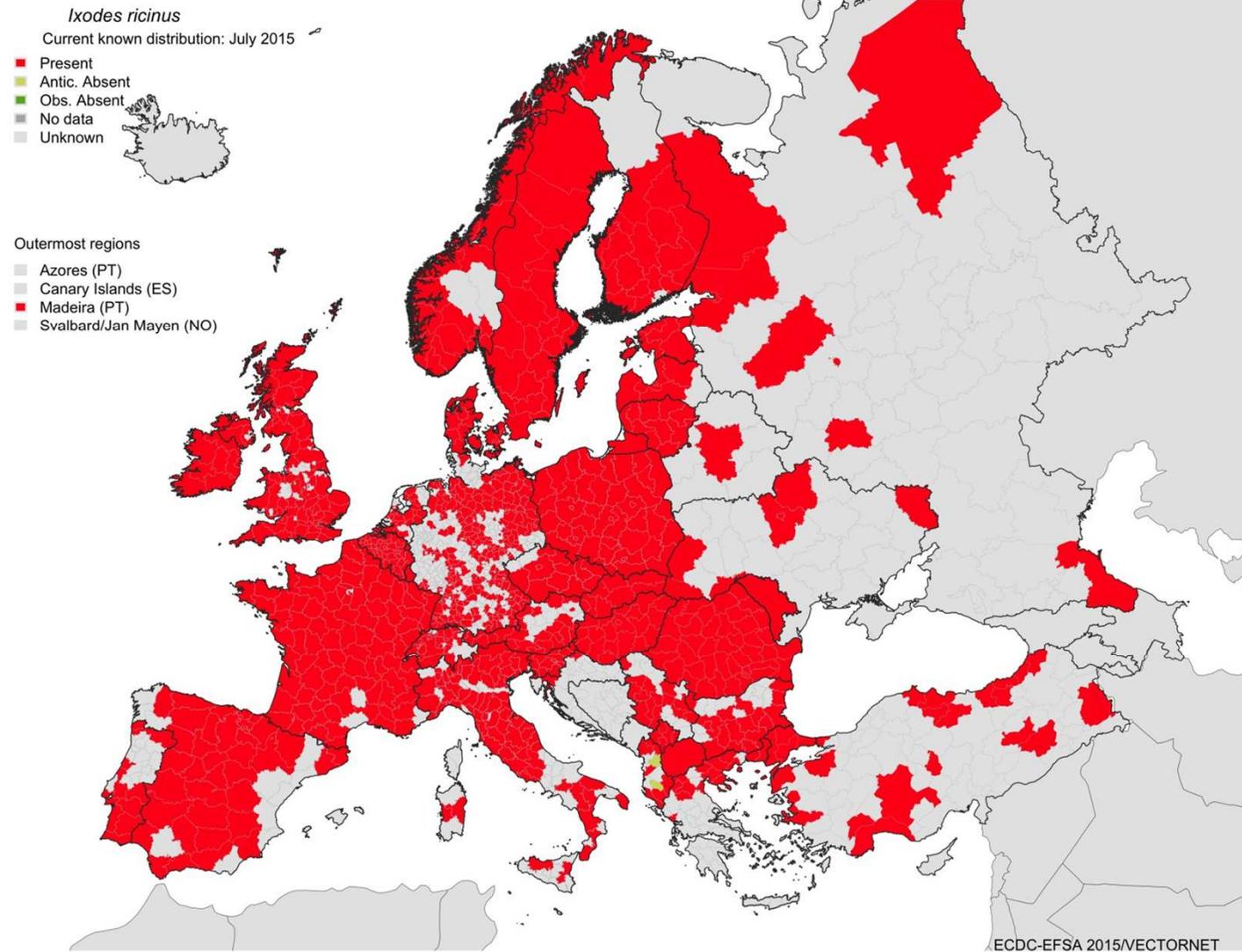
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Emerging Infectious Disease Agents

TRANSFUSION August 2009 Supplement Appendices

TRANSFUSION August 2009 Supplement Fact Sheets

Fact Sheets Created or Updated Post Publication of the TRANSFUSION August

Emerging Infectious Disease Agents and their Potential Threat to Transfusion Safety

The August 2009 issue of TRANSFUSION included a Supplement on emerging infectious disease (EID) agents and their potential threat to transfusion safety. Members of AABB's Transfusion Transmitted Diseases (TTD) Committee identified 68 infectious agents and described them in detail, including dengue, chikungunya and H1N1 influenza viruses, *Plasmodium* and *Babesia* species and the vCJD prion. The Supplement provides a set of tools identifying, describing, and prioritizing EID agents that have an actual or potential risk of transmission by transfusion and for which there is no currently implemented intervention.

The Supplement's 68 fact sheets include background information about each agent, along with a variety of assessments such as the clinical features of the agent and those characteristics specifically related to transfusion transmission. The fact sheets do not represent regulatory requirements, but instead serve as a starting point for developing policies.

Consensus opinions about prudent approaches (such as donor deferral periods) are included wherever possible based on facts that are currently inferred or known. Additionally, the agents are ranked according to the consensus opinion about their anticipated impact upon blood safety using scientific data and data related to the public perception of the agent.

Also included are tables summarizing the agents by agent category, priority ratings, those documented to be

Print

Fact Sheets Created or Updated Post Publication of the TRANSFUSION August 2009 Supplement

Fact Sheets Created Post Publication of the TRANSFUSION August 2009 Supplement

- Middle East Respiratory Syndrome Coronavirus created July 2013 (PDF)
- Human Parvovirus PARV4 created January 2013 (PDF)
- Measles (Rubeola) created October 2011 (PDF)
- Miscellaneous Arboviruses created October 2011 (PDF)
- Xenotropic Murine Leukemia Virus-Related Virus (XMRV) and other Polytropic Murine Leukemia Viruses (pMLV) updated October 2012 (PDF)
  - Table of Published Studies on XMRV and pMLV Findings in Human Diseases and the General Population updated September 2012 (PDF)
- Yellow Fever Virus and Yellow Fever Vaccine created March 2011 (PDF)

Fact Sheets Updated after Original Publication (original versions of each fact sheet are available in the TRANSFUSION August 2009 Supplement)

- Chikungunya Virus updated February (previously published in TRANSFUSION) (PDF) **NEW!**
- Dengue Viruses updated February 2014 (previously published in TRANSFUSION) (PDF) **NEW!**
- Hepatitis E Virus updated February 2014 (previously published in TRANSFUSION) (PDF) **NEW!**
- *Anaplasma phagocytophilum* updated July 2013 (previously published in TRANSFUSION) (PDF)
- *Babesia* Species updated July 2013 (previously published in TRANSFUSION) (PDF)
- *Ehrlichia* Species updated July 2013 (previously published in TRANSFUSION) (PDF)
- Hepatitis A Virus updated July 2013 (previously published in TRANSFUSION) (PDF)
- Human Parvovirus B19 updated January 2013 (previously published in TRANSFUSION) (PDF)
- *Bartonella* Species updated February 2012 (previously published in TRANSFUSION) (PDF)
- Chronic Wasting Disease (CWD) updated October 2011 (previously published in TRANSFUSION) (PDF)
- Human Prion Diseases (Other than vCJD) updated October 2011 (previously published in TRANSFUSION as CJD) (PDF)
- Variant Creutzfeldt–Jakob Disease (vCJD) updated October 2011 (previously published in TRANSFUSION) (PDF)
- Coxiella burnetii (Q fever) updated December 2010 (previously published in TRANSFUSION) (PDF)
- Japanese Encephalitis Virus Complex updated December 2010 (previously published in TRANSFUSION) (PDF)
- Tick-Borne Encephalitis Virus Complex updated December 2010 (previously published in TRANSFUSION) (PDF)

Return to Emerging Infectious Disease Agents

How do you manage 80 odd diseases?

- Never a status quo, always new outbreaks

- Cannot act on every change

- Lots of unknowns

*How to prioritize these (and novel) infectious diseases?*

What are the most important risk drivers?

University Medical Center Utrecht

Four most influential factors for transfusion transmission risks:

1) Transmissibility by transfusion

2) Disease impact

3) Prevalence of infection

4) Asymptomatic infectivity

Four most influential factors for transfusion transmission risks (model input variables):

1) Transmissibility by transfusion ?

Description	Range
Very unlikely	0.01-0.25
Unlikely	0.01-0.50
Unknown	0.01-0.99
Possible	0.25-0.75
Likely	0.50-0.99
Very likely	0.75-0.99

2) Disease impact ?

Description	Range
Very unlikely	0.01-0.25
Unlikely	0.01-0.50
Unknown	0.01-0.99
Possible	0.25-0.75
Likely	0.50-0.99
Very likely	0.75-0.99

3) Prevalence of infection ?

1 in
100,000-1,000,000
10,000-1,000,000
100-1,000,000
1,000-100,000
100-10,000
100-1,000

4) Asymptomatic infectivity ?

Description	Range
Very unlikely	0.01-0.25
Unlikely	0.01-0.50
Unknown	0.01-0.99
Possible	0.25-0.75
Likely	0.50-0.99
Very likely	0.75-0.99

- Pending exercise - Current exercise - Completed exercise

Hypothetical Disease Rankings

The point value represents the average risk of certain characteristics whereas the range values represent its underlying uncertainty. For each group, please rank the EIDs from highest risk to lowest, by placing each of them using the left-mouse-button (drag and drop) under the "Response" column. You can further re-order the Response column by drag and drop the EIDs. So upon completion, the EID with the highest priority should be ranked as 1 and the EID with the least priority should be ranked as 4.

EID	Prevalence of infection	Transfusion transmissibility	Asymptomatic phase	Disease impact	Total risk
A	1 in 100 to 1 in 1,000	0.875 (0.75-0.99)	0.125 (0.01-0.25)	12.5% (1%-25%)	1.6%(0.0056%-6.1%)
C	1 in 100,000 to 1 in 1,000,000	0.125 (0.01-0.25)	0.875 (0.75-0.99)	87.5% (75%-99%)	1.6%(0.0056%-6.1%)
B	1 in 100,000 to 1 in 1,000,000	0.5 (0.01-0.99)	0.5 (0.25-0.75)	25% (1%-50%)	0.83%(2.5E-05%-9.3%)
D	1 in 10,000 to 1 in 1,000,000	0.5 (0.25-0.75)	0.125 (0.01-0.25)	50% (1%-99%)	0.83%(2.5E-05%-9.3%)

Response rank order by expert 1:
1 – C
2 – A
3 – D
4 – B

Response rank order by expert 2:
1 – C
2 – A
3 – B
4 – D

Back   G1 G2 G3 G4 G5 G6   Next

Elicited outcomes

| Choice	Rank 1	Rank 2	Rank 3	Rank 4
A	13 (81%)	0 (0%)	2 (13%)	1 (6%)
B	0 (0%)	1 (6%)	3 (19%)	12 (75%)
C	1 (6%)	6 (38%)	7 (44%)	2 (13%)
D	2 (13%)	9 (56%)	4 (25%)	1 (6%)
E	15 (94%)	1 (6%)	0 (0%)	0 (0%)
F	0 (0%)	4 (25%)	9 (56%)	3 (19%)
G	1 (6%)	9 (56%)	3 (19%)	3 (19%)
H	0 (0%)	2 (13%)	4 (25%)	10 (63%)
I	12 (75%)	0 (0%)	1 (6%)	3 (19%)
J	1 (6%)	9 (56%)	4 (25%)	2 (13%)
K	3 (19%)	3 (19%)	7 (44%)	3 (19%)
L	0 (0%)	4 (25%)	4 (25%)	8 (50%)
M	10 (63%)	6 (38%)	0 (0%)	0 (0%)
N	1 (6%)	0 (0%)	8 (50%)	7 (44%)
O	4 (25%)	7 (44%)	1 (6%)	4 (25%)
P	1 (6%)	3 (19%)	7 (44%)	5 (31%)
Q	1 (6%)	6 (38%)	3 (19%)	6 (38%)
R	2 (13%)	3 (19%)	7 (44%)	4 (25%)
S	13 (81%)	2 (13%)	0 (0%)	1 (6%)
T	0 (0%)	5 (31%)	6 (38%)	5 (31%)
U	10 (63%)	5 (31%)	0 (0%)	1 (6%)
V	1 (6%)	0 (0%)	11 (69%)	4 (25%)
W	5 (31%)	10 (63%)	1 (6%)	0 (0%)
X	0 (0%)	1 (6%)	4 (25%)	11 (69%)

For each hypothetical disease is known:
- Transmission probability
- Disease impact
- Prevalence
- Asymptomatic infectivity

Weights for each variable and factor level

Risk weights derived
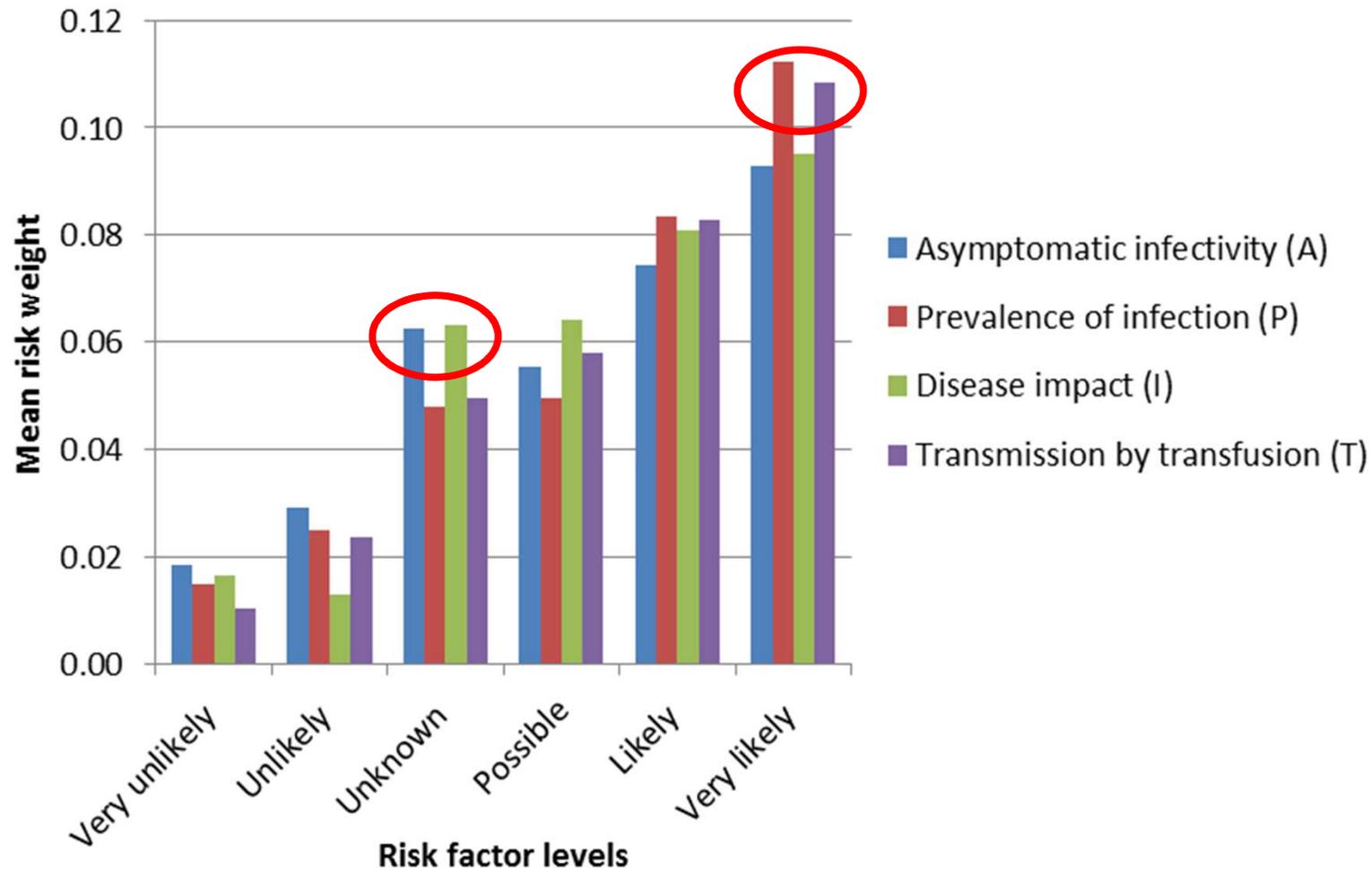
Contribution of "Very Certain" scores to high risks per influencing factor
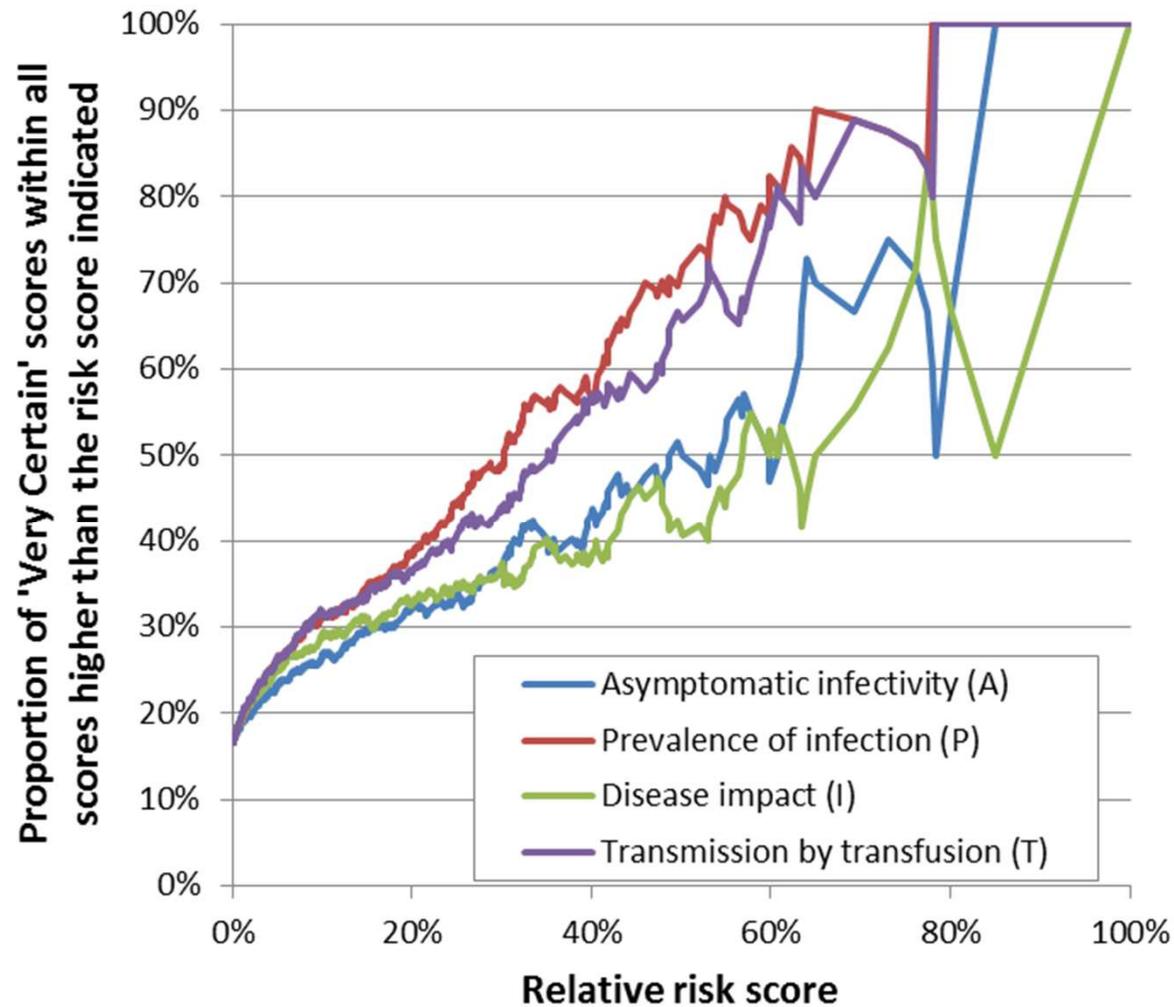
# Contribution of "Unknown" scores to high risks per influencing factor
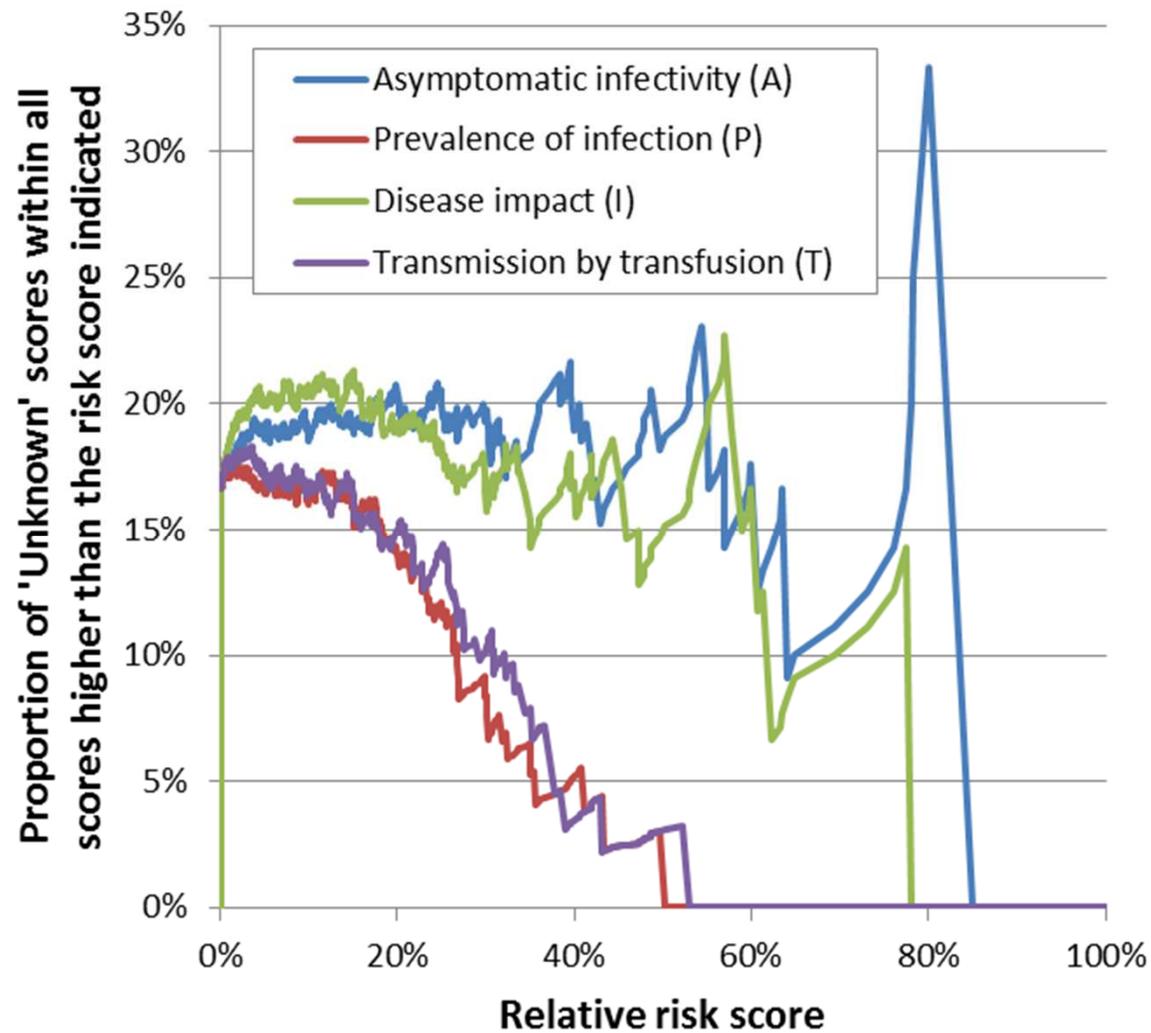
Ranking known diseases
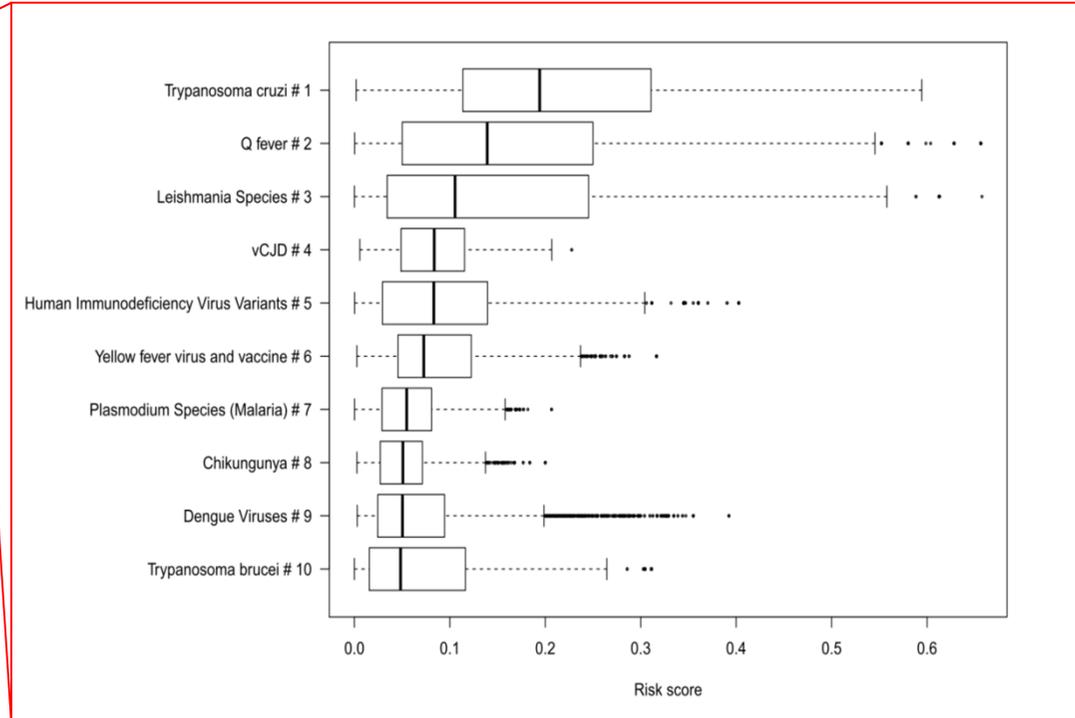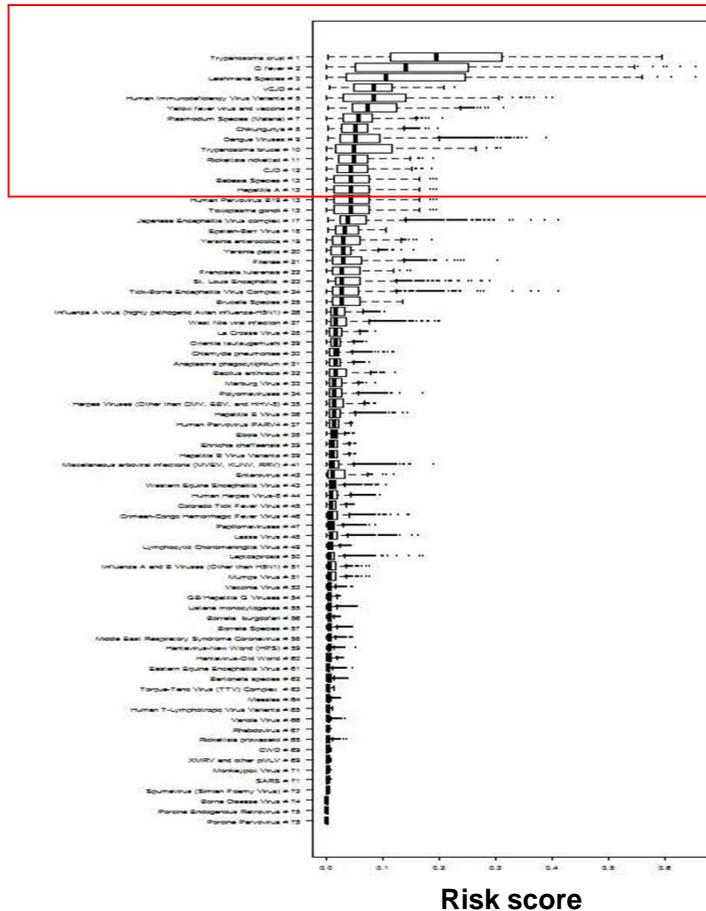
Objective and verifiable ranking by 16 experts in the field

So what's the point?

How would you rank the risk from a disease with:

- Likely transfusion transmissibility (50-100%)
- High disease impact (50-100%)
- Unknown prevalence (1/100-1/1000 000)
- Unknown asymptomatic phase (0-100%)

Ranking tool score:

Rank 3

Summary

1. We've developed a generic model to rank known or unknown newly emerging infectious diseases with respect to their risk to the blood supply

2. The model provides an objective means to support justification of safety investments

3. The model is implemented in an easy to use Excel spreadsheet and is available upon request.

4. Model should be more extensively validated and can be further refined.

Many thanks to....

- **Collaborators:**
  - Rabin Neslo, PhD (UMC Utrecht)
  - Welling Oei, MSc (UMC Utrecht / Sanquin Blood Supply)
  - Mirjam Kretzschmar, PhD (UMC Utrecht / RIVM)
  - Jim van Steenbergen PhD (RIVM)
  - Hans Zaaijer (Sanquin Blood Supply)
  - Cees vd Poel, PhD (UMC Utrecht / Sanquin Blood Supply)
  - Roel Coutinho (UMC Utrecht)

- **And the experts:** Ryanne Lieshout, Hans Zaaijer, Susan Stramer, Roger Dodd, Steve Kleinman, F. Blaine Hollinger, Dragoslav Domanovic, Philip Kiely, Villie Flari, Giovani Vandewalle, Susanne Ekblom-Kullberg, Salvador Oyonarte, Sheila MacLennan, Christine Saura, Kai Hourfar, Jason Acker

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❯ Lees verder

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Ik geef bloed

Producten & Diensten
Plasmaproducten

Onderwijs
Opleidingscatalogus

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Questions?

Cost-effectiveness of various screening tests in the Netherlands

Screening test	Screening costs [€]	Cases prevented	QALYs gained	Costs prevented [€]	ICER [€ per QALY]
Triplex MP6-NAT	8,178,609	3.22	1.57	9,924	5,199,220
Triplex ID-NAT	8,777,832	3.66	1.89	12,556	4,647,062
HAV NAT	578,367	1.06	0.031	369	18,562,483
HTLV antibody test, new donors only	25,665	2.22	0.011	214	2,234,041
~~HTLV antibody test, all donors~~	*** ABANDONED July 2013 ***				~~45,182,666~~
HTLV antibody test, pediatric recipients	114,417	0.24	0.004	61	26,984,140

Human T-lymphotropic (leukemia) virus or **human T-cell lymphotropic virus (HTLV)**

Cost-effectiveness of additional blood screening tests in the Netherlands. Borkent-Raven BA, Janssen MP, van der Poel CL, *et al.* Transfusion. Article first published online: 31 AUG 2011.