Adverse reactions and adverse events in blood donors: an international approach to the standardisation of classification

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International Haemovigilance Network
Sanquin Blood Supply
TRIP Hemovigilance and biovigilance

Donor (hemo)vigilance

Donor hemovigilance is the systematic monitoring of adverse reactions and incidents in the whole chain of blood donor care, with a view to improving quality and safety for blood donors.

From Haemovigilance: an effective tool for improving transfusion practice, RRP de Vries, P Robillard and JC Faber (eds), Wiley, 2012.

Definitions

2011 (IHN, ISBT)
Standard for the surveillance of complications related to blood donation

2014 (December) (IHN, ISBT and AABB)

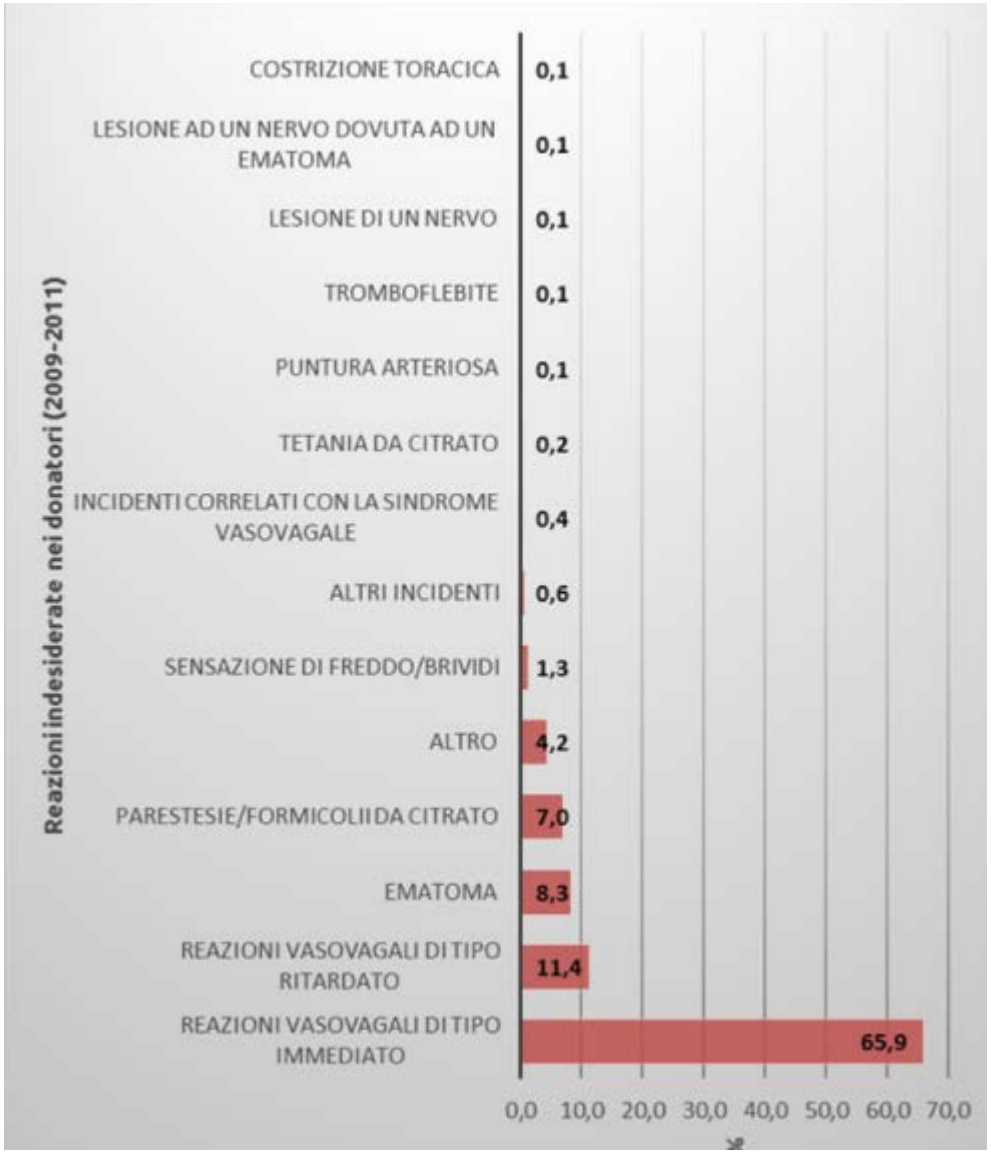
Revised classification for surveillance of complications of blood donation

- ✓Harmonised with AABB/DonorHART
- ✓Publicly available on IHN/ISBT websites
- ✓Endorsement
  - European Blood Alliance
  - Alliance of Blood Operators
  - WHO informed

Benefit of definitions

Harmonised definitions can contribute to improved donor care:

- Adequate, fact-based information for all donors
  - how often they occur
  - advice for recovery
  - tips for avoiding them
- Designing, implementing and evaluating preventive measures
- Research, comparisons, learning from best practices.



Chest pain or tightness

Haematoma/nerve irritation

Nerve injury

Thrombophlebitis

Arterial puncture

Citrate reaction (tetany)

Vasovagal reaction + accident

Other accident

Sensation of cold/ shivers

Other

Tingling from citrate reaction

Haematoma

Delayed vasovagal reaction

Immediate type vasovagal reaction

Istituto Superiore di Sanità

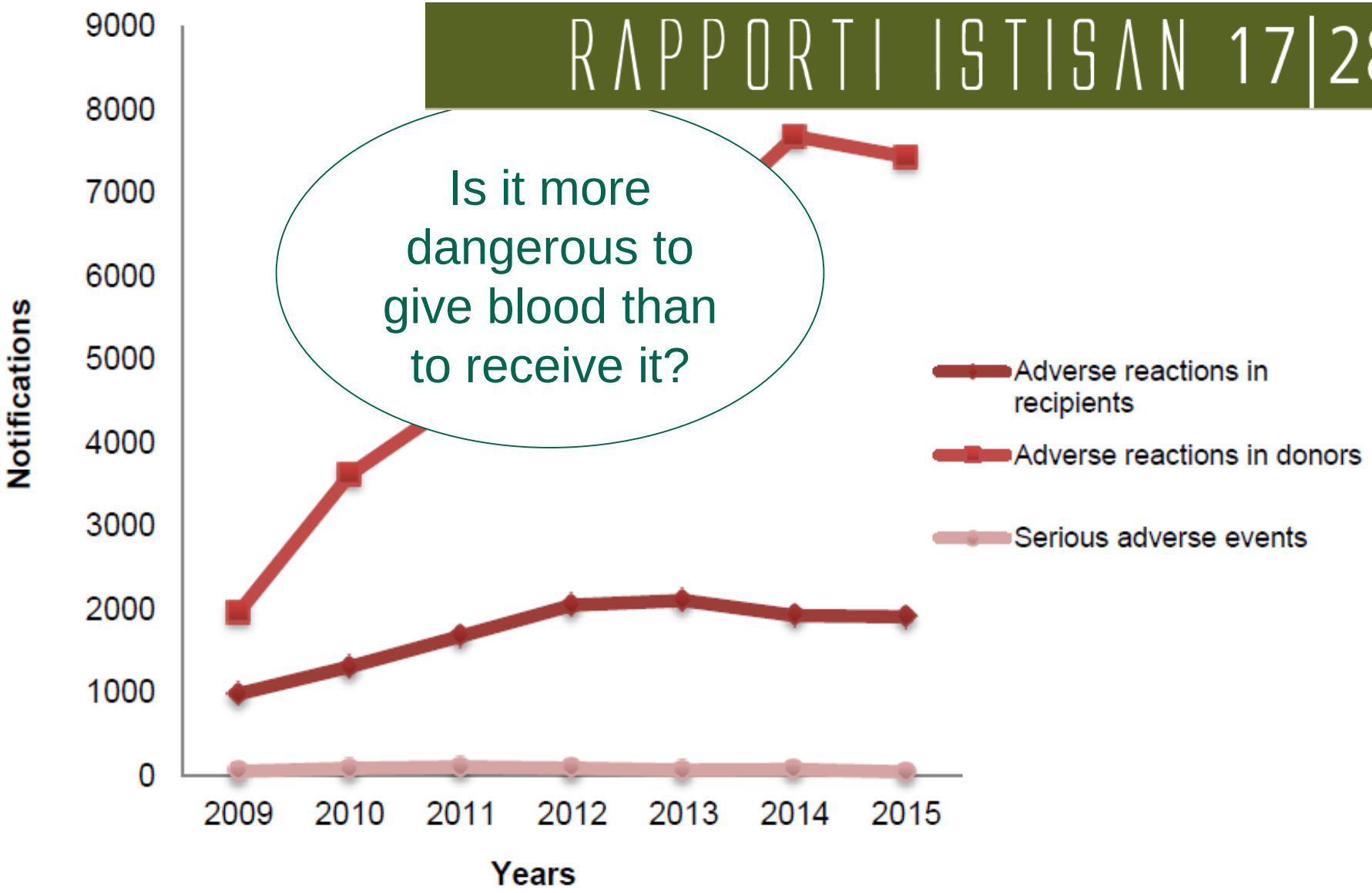
Attività di emovigilanza in Italia. Rapporto 2015.

"…. In 2015, 7,435 adverse reactions to homologous donation were notified (1 every 411 donations), 1,054 of which were severe (1 every 2,904 donations). The highest frequency of reactions was related to apheresis donations compared to whole blood donations. The most frequent type of notified reaction was the immediate vasovagal reaction (72.8%), of which only 4.3% were severe."

Rate with apheresis (all reactions):	4,1/1000 procedures
Rate with whole blood donation:	2,1/1000 collections

652 haematomas reported, all severe

Compared to 311 severe vasovagal reactions



NB all severity levels of reactions are included

Figure 1. Haemovigilance: no. of notifications per year (2009-2015)

Comparing donor reaction data

	It 2015	NL 2017
Total donations	3061479	730273
All adverse reactions (per 1000)	7432 (2.4)	8868 (12.1)
Serious adverse reactions	955	10
Vasovagal immediate, all severities	5410	4111
VVR delayed, all severities	936	
VVR, severe (% of all VVR)	311 (4.9%)	7 (0.2%)
All reactions, whole blood (per 1000)	5480 (2.1)	5106 (12.2)
All reactions, apheresis (per 1000)	1955 (4.1)	3595 (12.1)
All VVR, rate_WBD (per 1000)		4602 (11.0)
All VVR, rate_apheresis (per 1000)		2352 (7.6)

Possible causes for differences

Rates known to differ between:

- Male – female donors
- First time vs more experienced, young vs older
- Whole blood vs apheresis
- Estimated blood volume, Hb
- Circumstances on day of donation etc.

More reactions

- If Hb higher
- If EBV lower

Differences in reporting:

- Reporting protocols, staff alertness/time to make report
- Assessment of severity

Note: this table shows annual rates *per donor*

Rapporti ISTISAN 17/28

Tabella 10. Donatori totali e donatori che hanno manifestato reazioni indesiderate alla donazione suddivisi per classi di età e per sesso (2015)

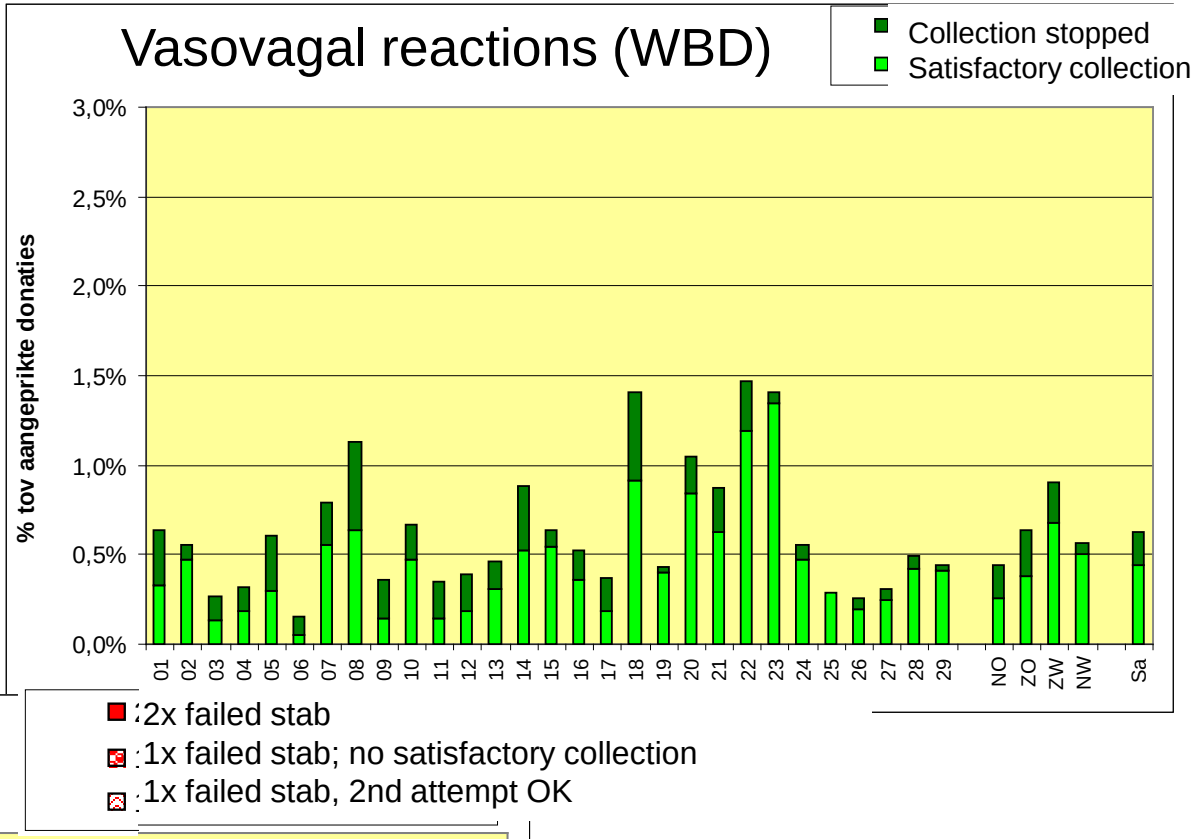
Classe d'età (anni)	Donatori con reazione indesiderata			Donatori totali			Donatori con reazione/ 1.000 donatori		
	M	F	totale	M	F	totale	M	F	totale
18-25	1.076	1.176	2.252	143.725	107.810	251.535	7,5	10,9	9,0
26-35	1.002	687	1.689	224.090	108.354	332.444	4,5	6,3	5,1
36-45	1.077	616	1.693	355.342	140.209	495.551	3,0	4,4	3,4
46-55	684	603	1.287	349.179	137.354	486.533	2,0	4,4	2,6
56-65	231	264	495	159.477	61.031	220.508	1,4	4,3	2,2
66 e oltre	9	10	19	9.544	2.595	12.139	0,9	3,9	1,6
Totale	**4.079**	**3.356**	**7.435**	**1.241.357**	**557.353**	**1.798.710**	**3,3**	**6,0**	**4,1**

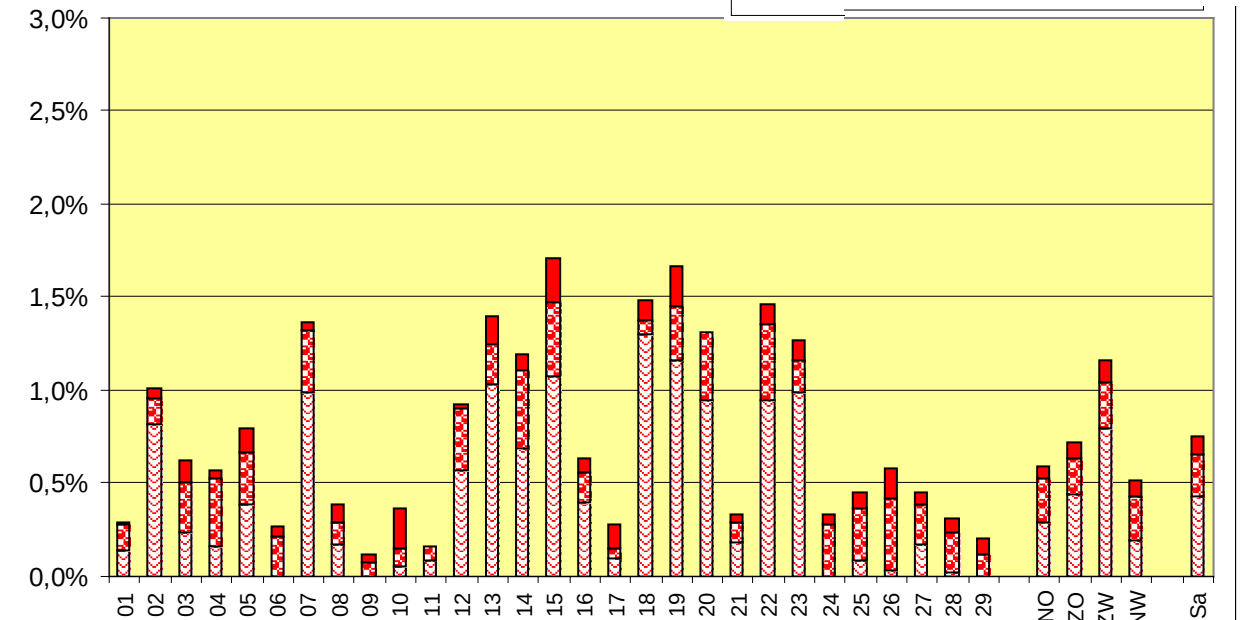
M: maschi. F: femmine
La tabella presenta anche l'indice dei donatori con reazioni ogni 1.000 donatori, che, stratificato per sesso e fasce di età, indica le donatrici di età compresa tra i 18-25 anni più soggette a sviluppare una reazione indesiderata.

Variation in 1st time%

Country	Regular and repeat donors	First time donors	% first time donors
Georgia	32 725	17 116	34.3
Germany	2 174 627	413 085	16.9
Greece	305 123	62 138	16.9
Hungary	220 656	51 822	19.0
Iceland	5 913	1 569	21.0
Ireland			
Italy	1 412 585	386 125	22.5
Latvia	24 329	8 658	26.2
Liechtenstein			
Lithuania	33 341	32 385	49.3
Luxembourg			
Malta	10 361	2 163	17.3
Moldova			
Montenegro			
Netherlands	230 907	34 160	9.9
Norway	99 263	20 814	21.0
Poland	475 134	113 585	18.0
Portugal	229 720	37 603	14.1
Romania			
Russian Federatio	998 663	511 788	33.9
San Marino			
Serbia			
Slovakia	112 592	27 906	19.9
Slovenia			
Spain	950 631	229 825	19.5
Sweden	219 380	45 435	17.2
Switzerland	200 062	28 170	12.3
Turkey			

Variation within organisation





Parameters and denominators recommended in new definitions

Recommended data about each reaction:

1. Type of complication

2. Gender of donor

3. Type of donation

Whole blood or Apheresis (*optional)*

4. First-time vs repeat donor

Age group of donors (optional)

IHN's International Surveillance database for Transfusion Adverse Reactions and Events in donors and recipients of blood components (ISTARE)

Working Group *C. Politis, C. Richardson, Ph. Renaudier, P. Robillard, M.A. Escoval, J. Wiersum*

Aggregate data from national HV systems

- Recipient adverse reactions (by blood component, severity, imputability
- Blood donation complications (WBD – apheresis)

ISTARE
INTERNATIONAL SURVEILLANCE OF TRANSFUSION-ASSOCIATED REACTIONS & EVENTS

2012-2016 data
(79 country years, 84.1 million donations)

	N Total	Rate per 100,000	N serious	% severe
Haematoma	91713	109	4589	5.0%
Arterial puncture	1176	1.4	52	4.4%
Delayed bleeding	1337	1.6	15	1.1%
Painful arm	16647	19.8	1440	8.7%
Localised infection	188	0.2	75	40%
Thrombophlebitis	260	0.3	137	53%
VVR Immediate type	334138	397	17161	5.1%
VVR Immediate type, accident	2744	3.3	1143	42%
VVR Delayed type	19284	22.9	1913	9.9%
VVR Delayed, accident	1034	1.2	354	34%
Citrate reaction*	8122	47	671	8.3%
Haemolysis*	38	0.1	9	24%
Generalised allergic reaction	94	0.1	41	44%
Air embolism*	12	0.05	5	42%
Other	10178	12.1	1254	12%

*rate per 100000 apheresis procedures

Severity

EU directive 2002/98

'Serious adverse reaction' shall mean an unintended response in **donor** or in patient associated with the collection or transfusion of blood or blood components that is fatal, life-threatening, disabling, incapacitating, or which results in, or prolongs, hospitalisation or morbidity

In the revised definitions

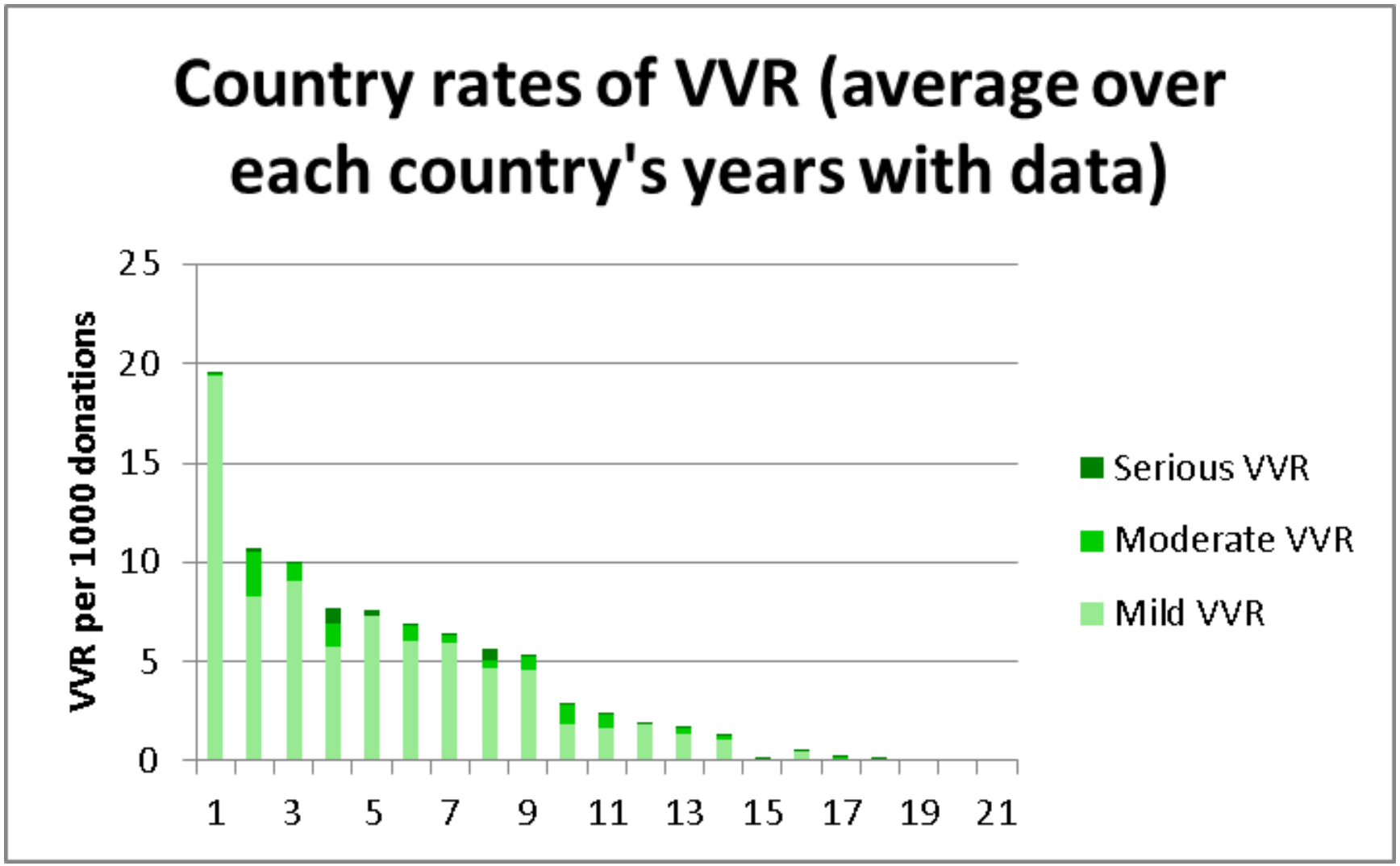
Grading of severity - optional

Life-threatening complications and long-term disability are thankfully extremely rare after blood donation. Grading of severity for donor reactions does not easily fit into grading systems used for adverse reactions in patients. Use of this grading system is therefore optional. The criteria for classification of a reaction as serious (severe) as derived from these systems are:

Hospitalization:	*If it was attributable to the complication. The criterion of hospital admission is applicable if a donor is kept in hospital overnight. Cases where a donor is seen, examined, and in some cases given treatment (e.g. suturing, IV fluids, treatment of a fracture) but discharged home are not automatically classified as serious.*
Intervention:	*To preclude permanent damage or impairment of a body function or to prevent death (life- threatening)*
Symptoms:	*Causing significant disability or incapacity following a complication of blood donation and persisted for more than a year after the donation (Long term morbidity)*
Death:	*If it follows a complication of blood donation and the death was possibly, probably or definitely related to the donation.*

ISTARE
INTERNATIONAL SURVEILLANCE OF TRANSFUSION-ASSOCIATED REACTIONS & EVENTS

2012-2016 data:
variation in severity assessment



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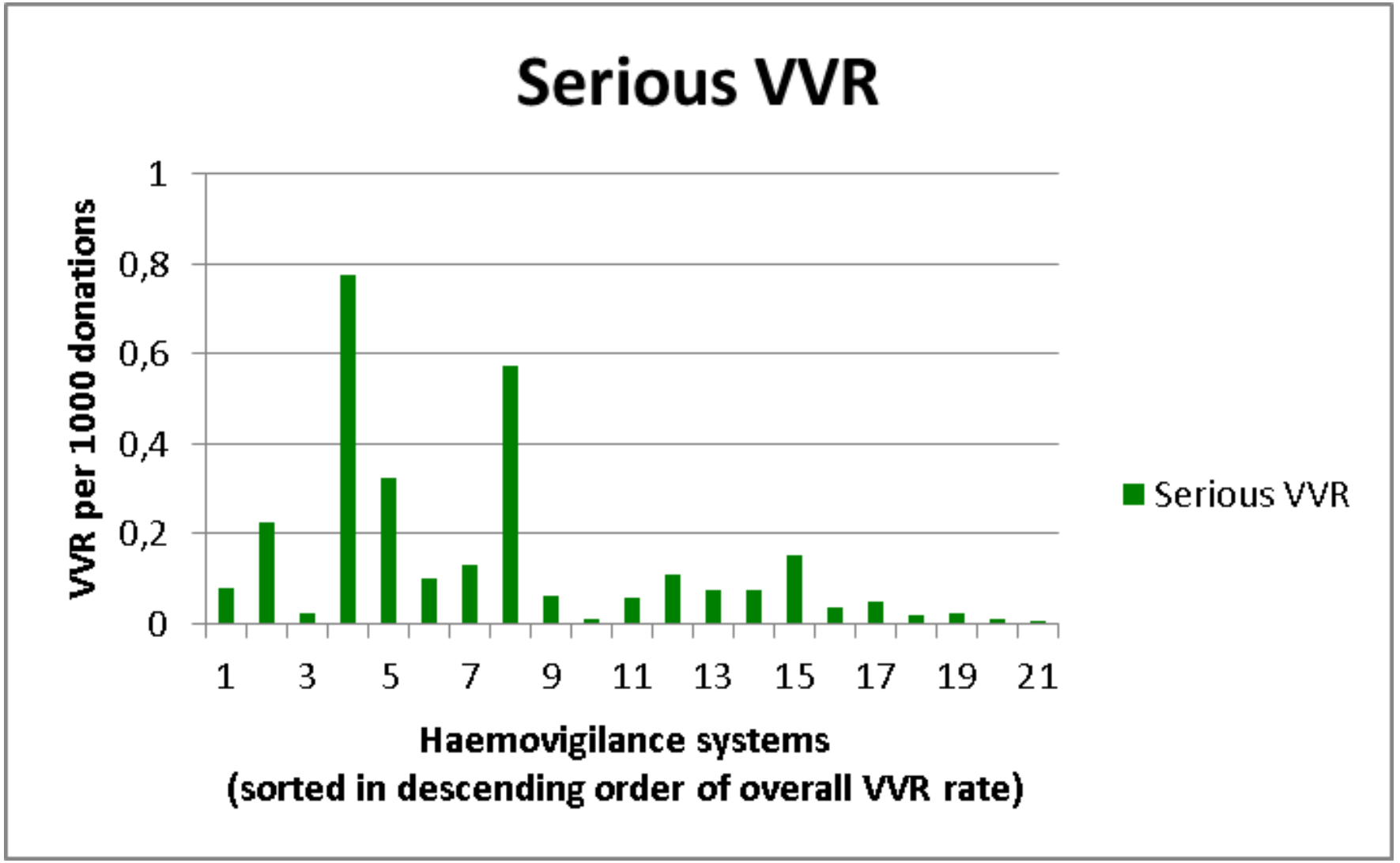

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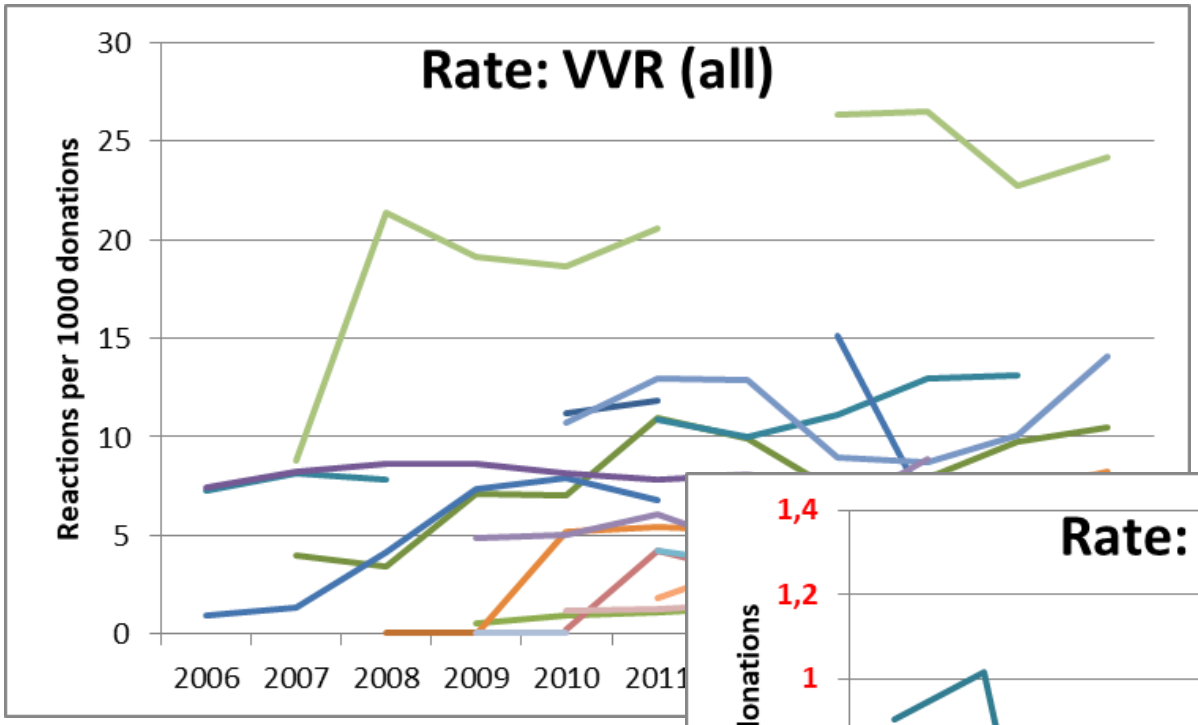

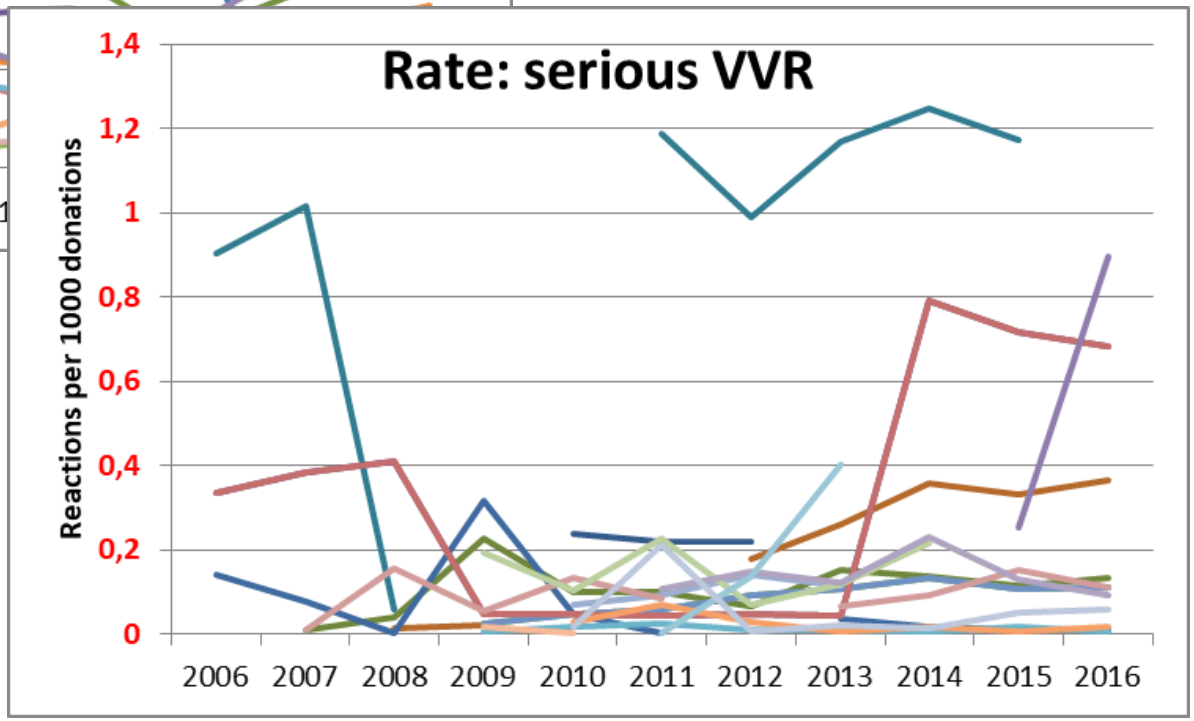

Advancing Transfusion and Cellular Therapies Worldwide

Grading Severity of Blood Donor Adverse Events Tool

AABB Donor Hemovigilance Working Group, 2018
Chair: Mary Townsend

- Tool is patterned after the (clinical) severity scale, Common Terminology Criteria for Adverse Events (CTCAE1) v 5.0
- Grades 1-5 are roughly associated with mild, moderate, severe, life-threatening and death
- Testing phase: Jan-February 2019

Advancing Transfusion and Cellular Therapies Worldwide

Draft (2018-9)

Severity Grade	General factors	(DAE) Examples
Grade 1	Resolved with no or minimal intervention ***AND*** • Short duration ≤ 2 weeks ***AND*** • No limitation on Activities of Daily Living (ADL) ***AND*** • No Outside Medical Care (OMC)	Vasovagal event that resolves with comfort care and/or oral hydration; Citrate reaction resolved with oral calcium or reduction in infusion rate
Grade 2	OMC, no hospitalization ***OR*** • Duration >2 weeks- ≤ 6 months ***OR*** • Limitations on ADL for ≤2 weeks	Superficial thrombophlebitis resolved with oral ntibiotics, no sequelae; Vasovagal event that requires transport to ER for IV hydration; Lacerations requiring sutures
	(Continued on next slide)	

Advancing Transfusion and Cellular Therapies Worldwide

Draft (2018-9)

Severity Grade*	General factors	(DAE) Examples
Grade 3	Hospitalization ***OR*** • Duration >6 months ***OR*** • Limitations on ADL >2 weeks ***OR*** • Require surgery of any kind	Arteriovenous fistula requiring surgical repair Fracture, dental injury, or concussion
Grade 4	Immediate medical intervention required to prevent death	Loss of consciousness, fall and intracranial bleed
Grade 5	Death related to DAE	

*Grade 4 and Grade 5 are not shown in the Grading Severity of Blood Donor Adverse Events Tool.

*Note difference from ISBT haemovigilance grades (1-4)

Female donor, 45 years old: uncomplicated (repeat) whole blood donation drank water + ate biscuit afterwards

- On street outside collection centre, she became dizzy and fell to ground
- Passer-by gave assistance, donor rapidly regained consciousness.
- Staff alerted. BP 85/45. Donor helped back to centre.
- Remained na… fluids over th…
- Ambulance c…
- Given 500 ml… evening
- NB no injury. …at evening and s…

- Outside medical care,
- Intervention
- No overnight hospital stay
- No longer term disability, no impact on ADL

Grade 1

✓ **Grade 2**

Grade 3

Grade 4

Grade 5

Grading Severity of Blood Donor Adverse Events Tool

- Next steps: Adjustments if necessary based on comments
- Publish and disseminate
- For the (EU, voluntary) reporting of serious adverse reactions in donors, is it possible to align?
  Currently: differences of practice!
  Some countries report Grades 2 and higher (as described in the Tool), some countries report Grades 3 and higher)

Work in progress!

Acknowledgements

All blood donors

IHN, ISTARE Working group, ISBT

Sanquin

Tanneke Marijt, all colleagues

ISBT haemovigilance working party

Kevin Land, Barbee Whitaker

AABB donor hemovigilance committee and severity subgroup

Chair: Mary Townsend

Thank you for inviting me

Thank you all for your attention