

Transfusion reactions reported to TRIP: a closer look at the allergic transfusion reactions

Jo Wiersum-Osselton, Anita van
Tilborgh, Pauline Zijlker, Martin
Schipperus

- Transfusion setting
- Hemovigilance in NL
 - Method
 - Allergic transfusion reaction definitions
- Overview of findings, 2002-2010
 - + Some preliminary 2011 data

Bp, interval, patients, symptoms, IgA

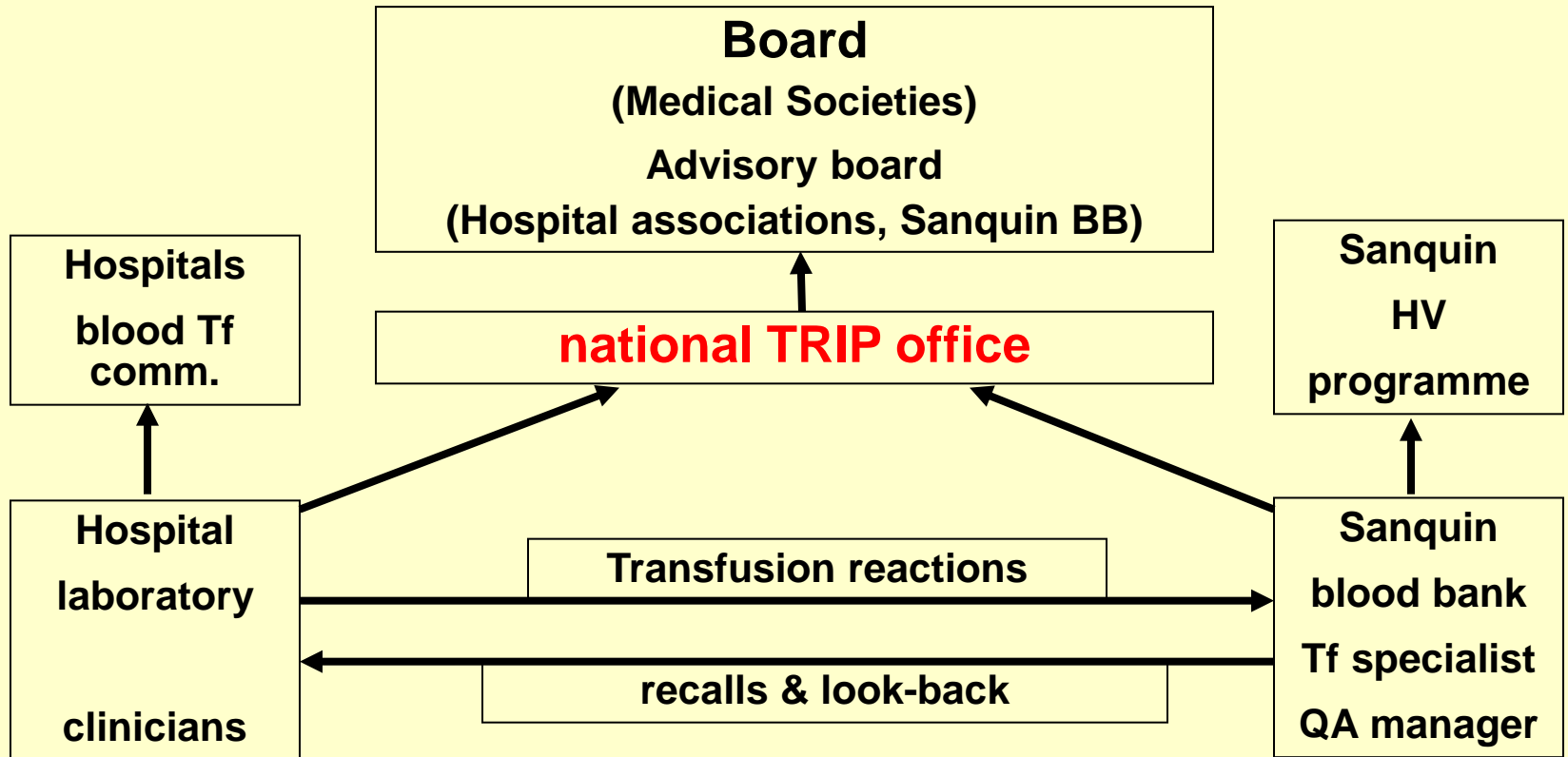
- Where next?

Blood supply

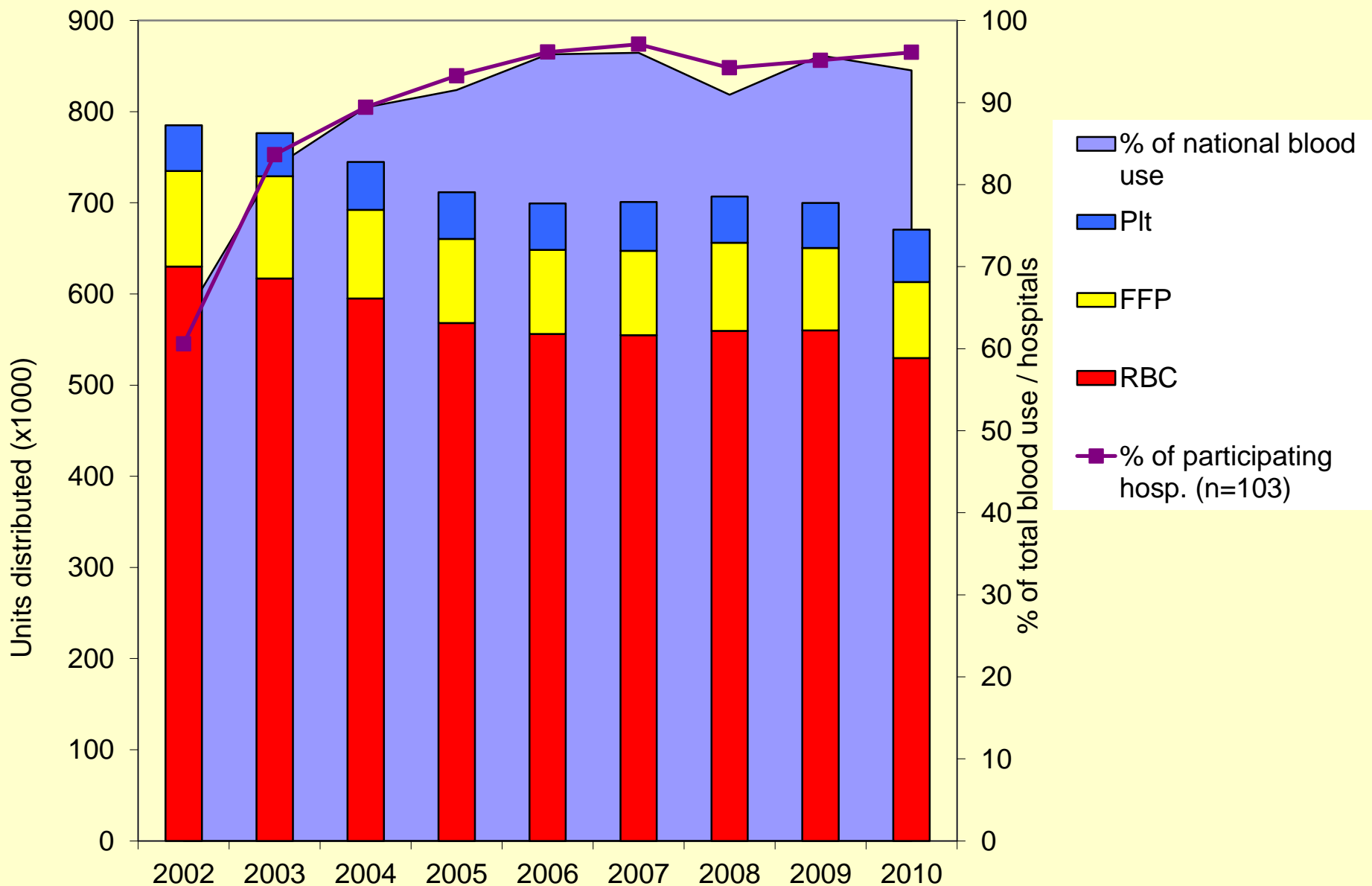
Population (millions)	NL (2010) 16.7
Donors x1000 Donations x1000	395
Whole blood	542
Apheresis	341
Hospitals	+/- 100
Units distributed (x1000)	
Red blood cells	534
Platelets	57
Plasma	83 (male Q-FFP)
Fractionation	348,000 kg

Platelets

- *pooled 5-D BC plts (plasma or PAS)
- *1/10 apheresis platelets
- *Bacteria screening
- *Shelf life 7 days



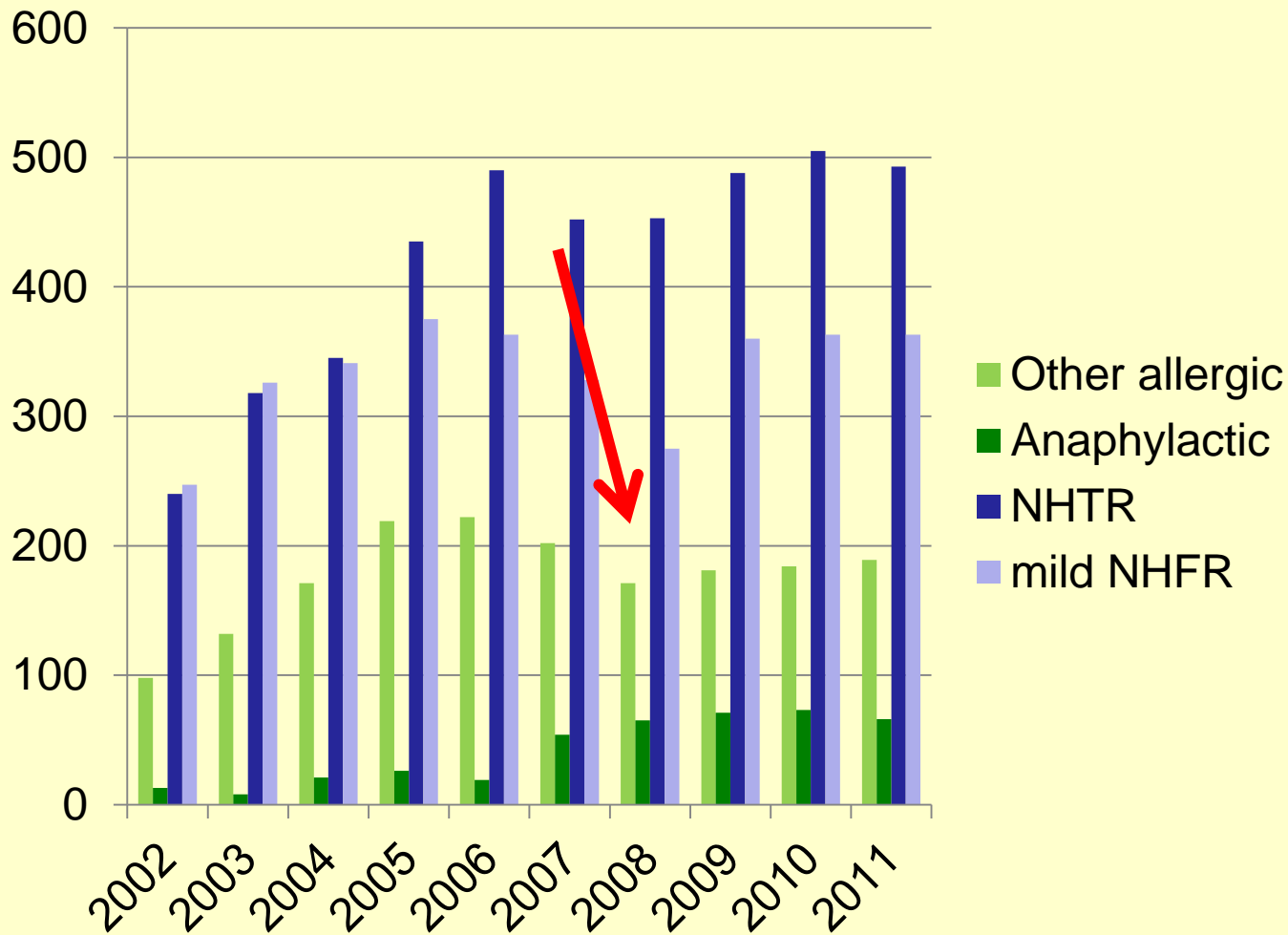
Annual blood use and HV reporting



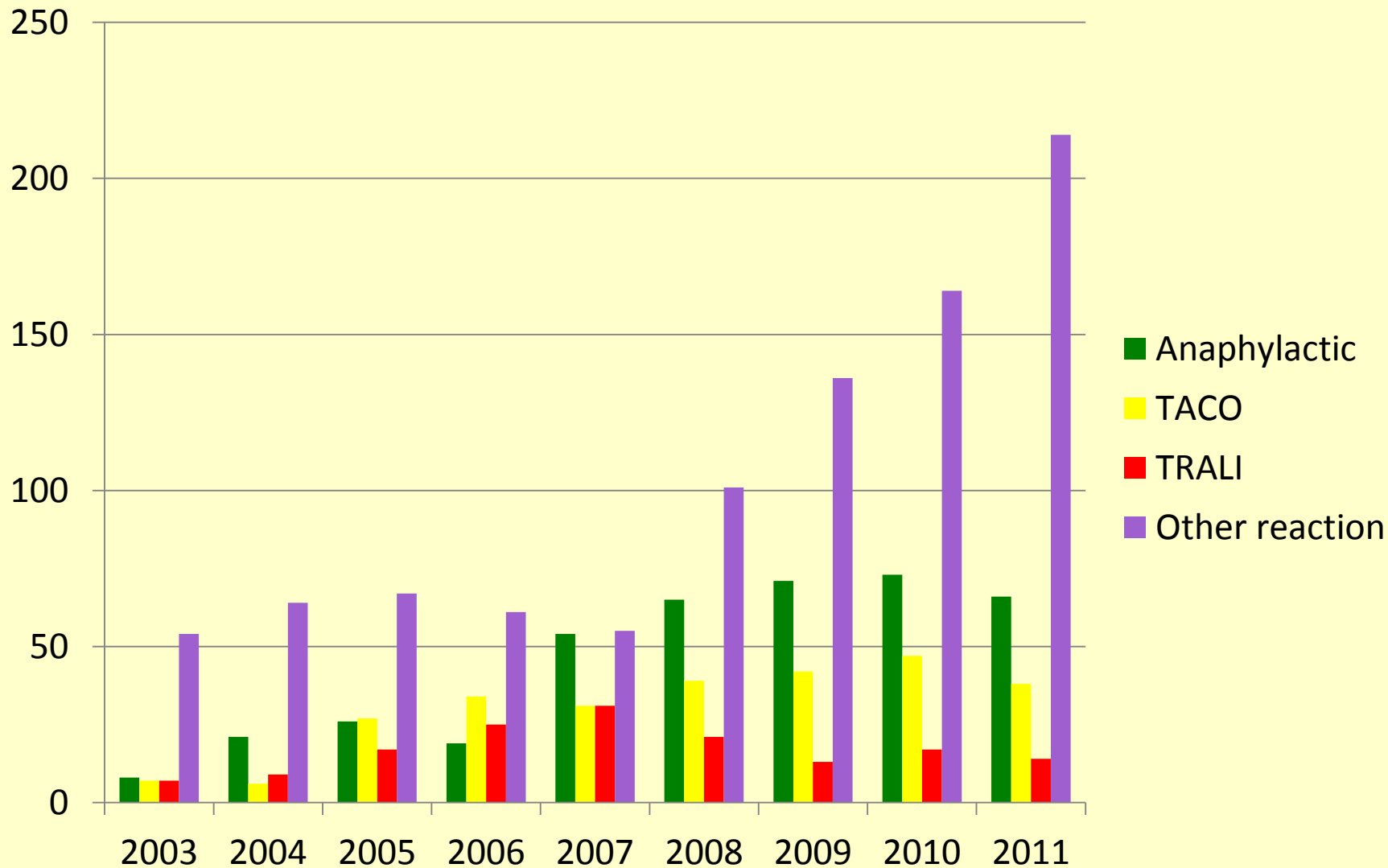


Transfusion reactions	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
AHTR	12	8	14	9	19	11	18	18	21	16
Anaphylactic	13	8	21	26	19	54	65	71	73	66
Other allergic	98	132	171	219	222	202	171	181	184	189
Hemosiderosis				4	5	3	5	2	4	2
Mild NHFR	247	326	341	375	363	328	275	360	363	363
NHTR	240	318	345	435	490	452	453	488	505	493
New allo-ab	117	244	428	571	607	601	610	756	814	826
Other reaction	48	54	64	67	61	55	101	136	164	214
Post-tf bacteremia	12	9	5	10	7	19	37	55	41	60
Post-tf other infection										1
PTP	1						1			2
Post-tf viral infection	1	5	7	8	7	7	7	4	1	5
TA-GVHD							1			
TRALI	9	7	9	17	25	31	21	13	17	14
Delayed HTR	21	19	14	12	14	11	18	8	7	9
TACO	1	7	6	27	34	31	39	42	47	38

Reports per year



Reports per year



TRIP definitions (2008)

Anaphylactic transfusion reaction

Rapidly developing reaction occurring within a few seconds to minutes after the start of transfusion, with features such as airway obstruction, in and expiratory stridor, fall in blood pressure ≥ 20 mm Hg systolic and/or diastolic, nausea or vomiting or diarrhoea, possibly with skin rash.

Investigations: Hemolysis testing and bacteriology negative, test for IgA and anti-IgA.

Other allergic reaction

Allergic phenomena such as itching, redness or urticaria but without respiratory, cardiovascular or gastrointestinal features, arising from a few minutes of starting transfusion until a few hours after its completion. Hemolysis testing and bacteriology negative if performed.

TRIP definitions (2008)

Anaphylactic

Rapidly developing
within a few seconds to minutes
after the start

Features such as airway
obstruction, in and expiratory stridor,
fall in blood pressure ≥ 20 mm Hg
systolic and/or diastolic, nausea or
vomiting or diarrhoea

possibly with skin rash

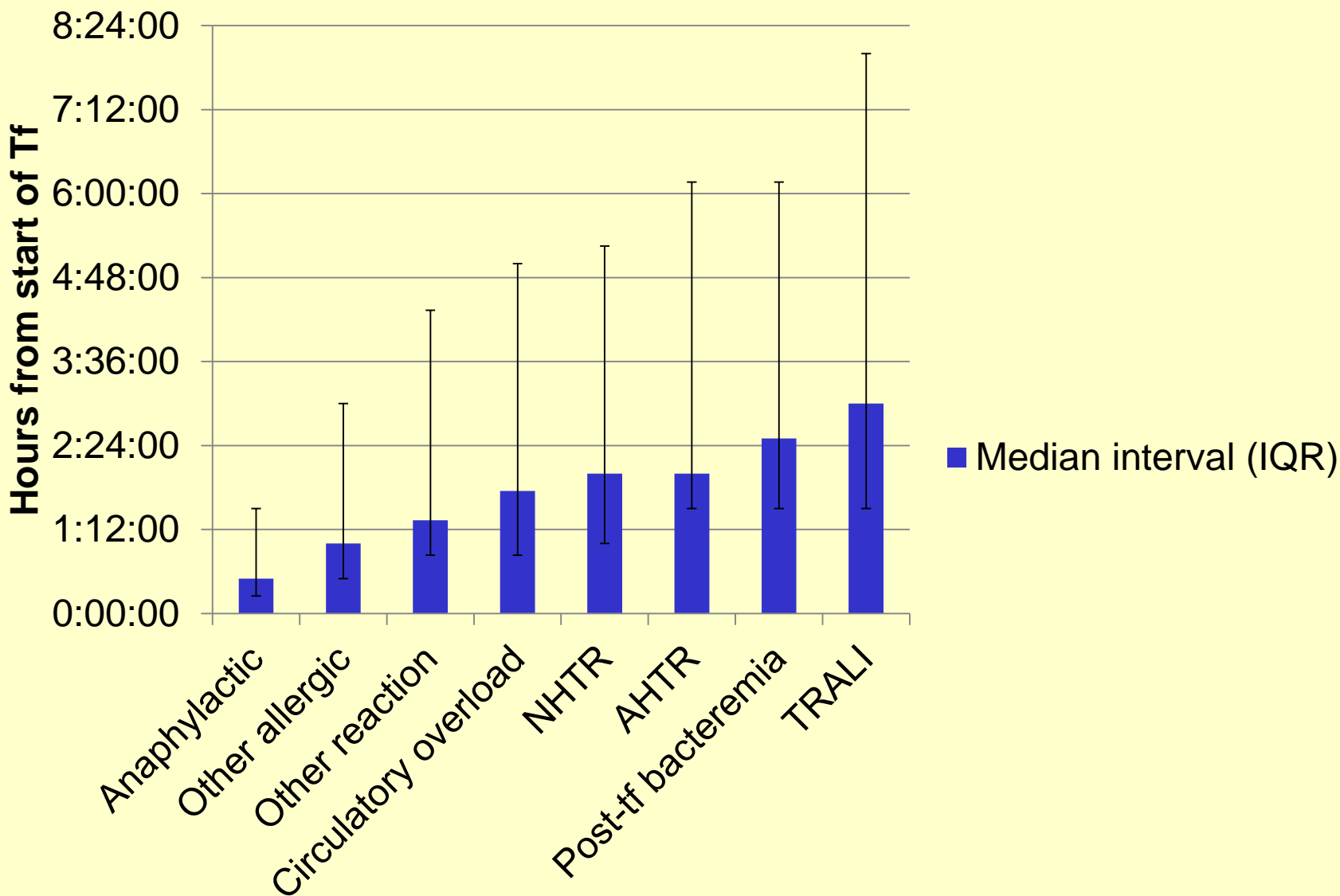
Other allergic

from a few minutes of starting
transfusion until a few hours after

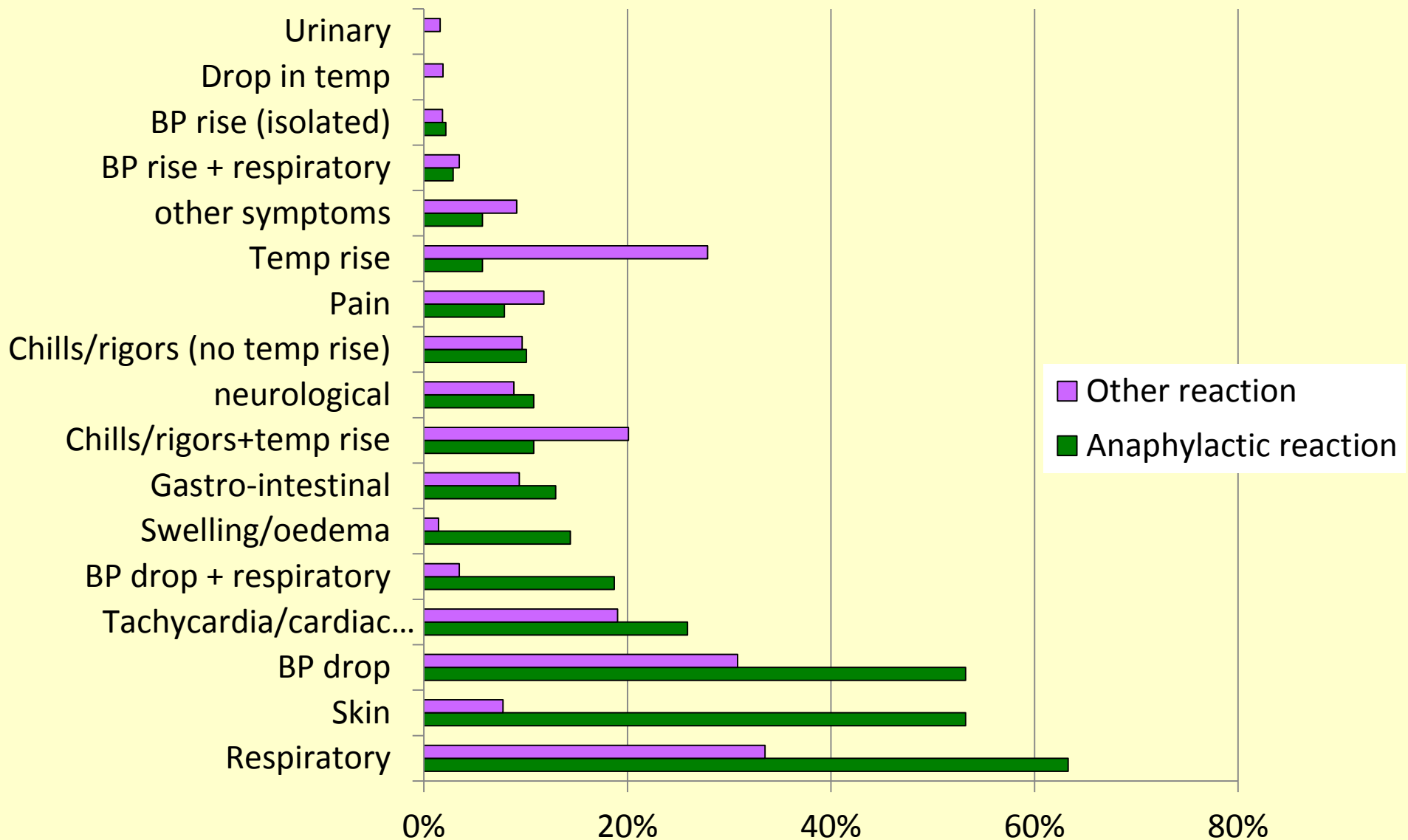
without respiratory, cardiovascular
or gastrointestinal features

Allergic phenomena such as itching,
redness or urticaria

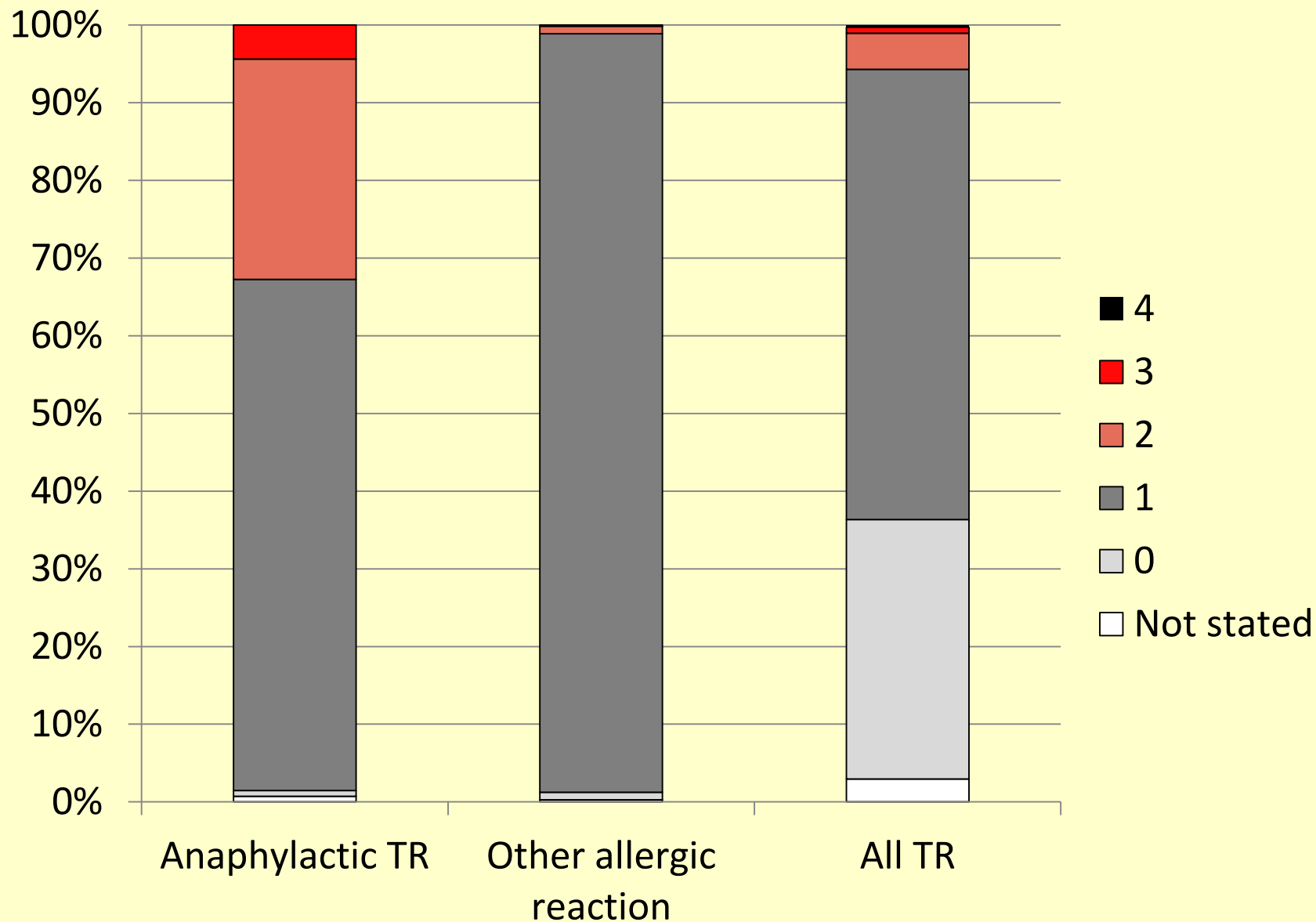
Rapidly developing...



Symptoms



Severity (2008-2011)

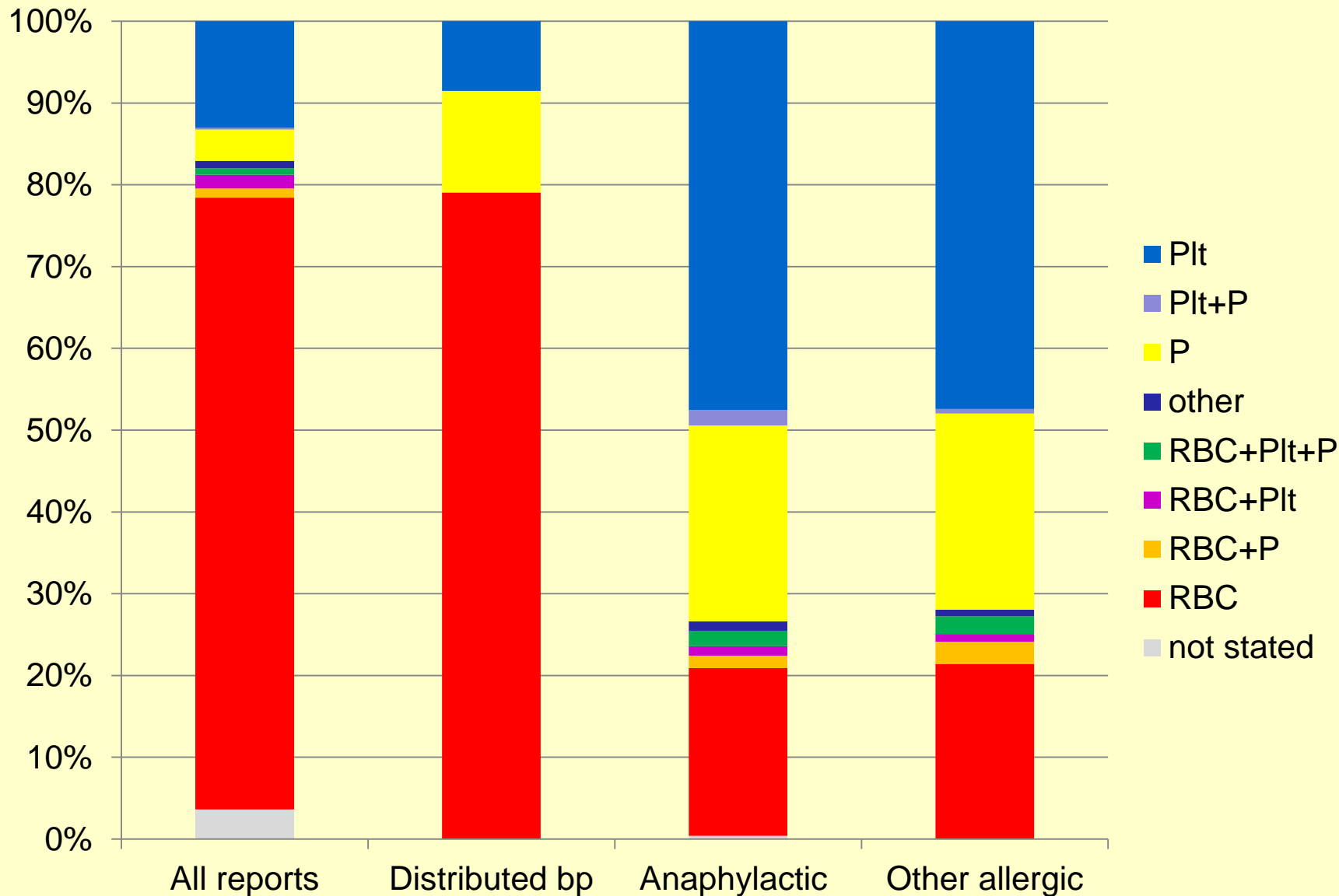




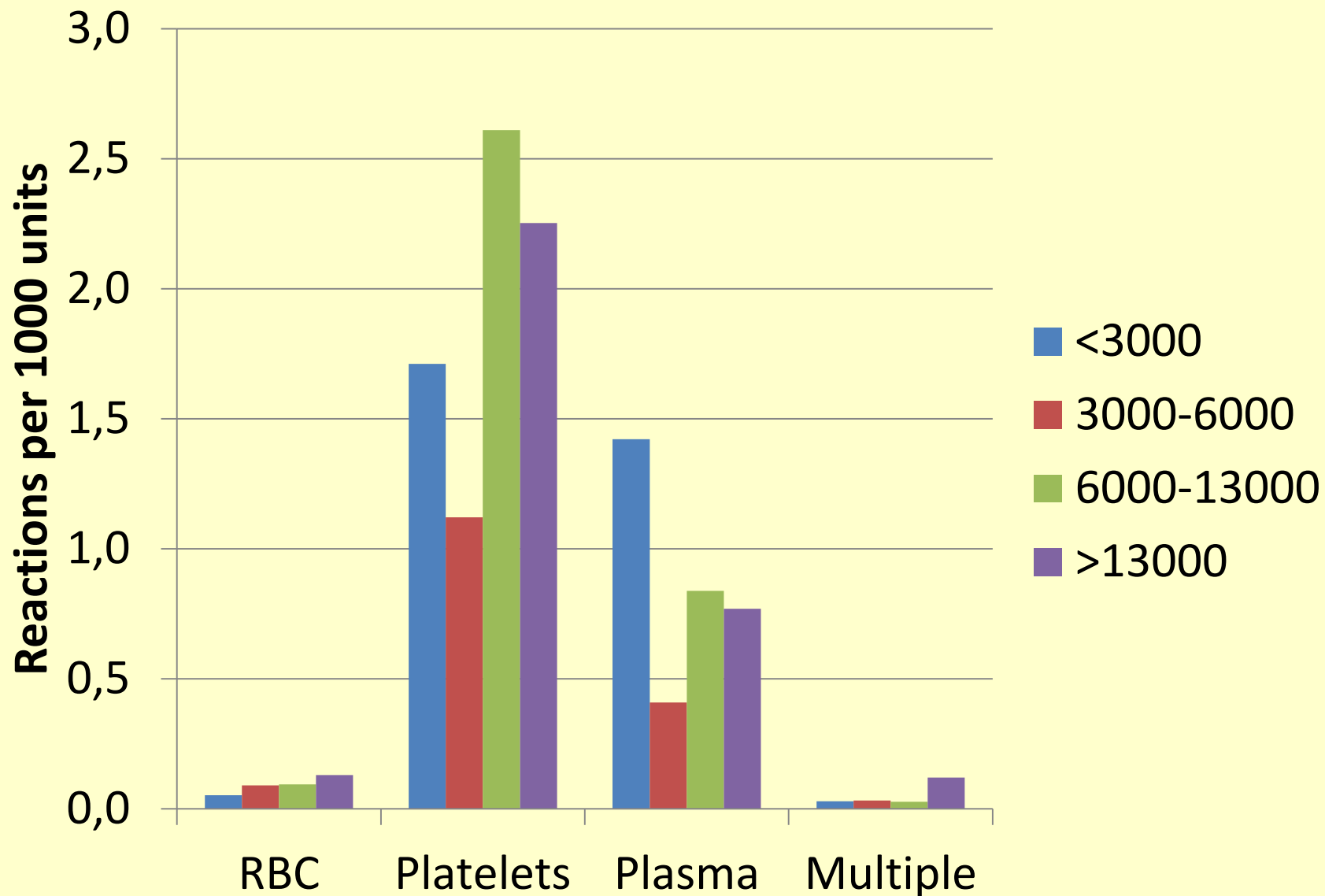
Grade 4 (definite, probable or possible)

Category	No.	Years
Acute hemolytic TR	3	2003, 2009, 2011
Anaphylactic	2	2005, 2007
Bacterial contamination Post-transfusion bacteremia/sepsis	2	2003, 2009
Other reaction	7	2002, 2005, 2008, 2010, 2011
TRALI	9	2005, 2006, 2007, 2009, 2010
Transfusion-associated circulatory overload	1	2005, 2006, 2010, 2011
Incorrect blood component transfused	1	2008

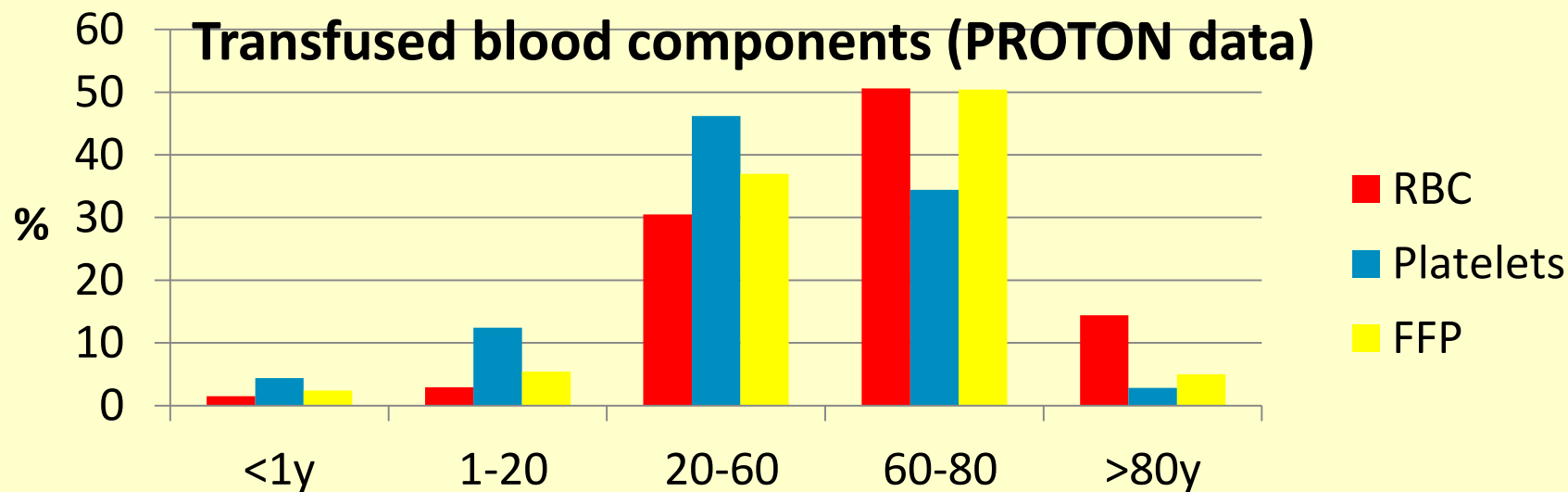
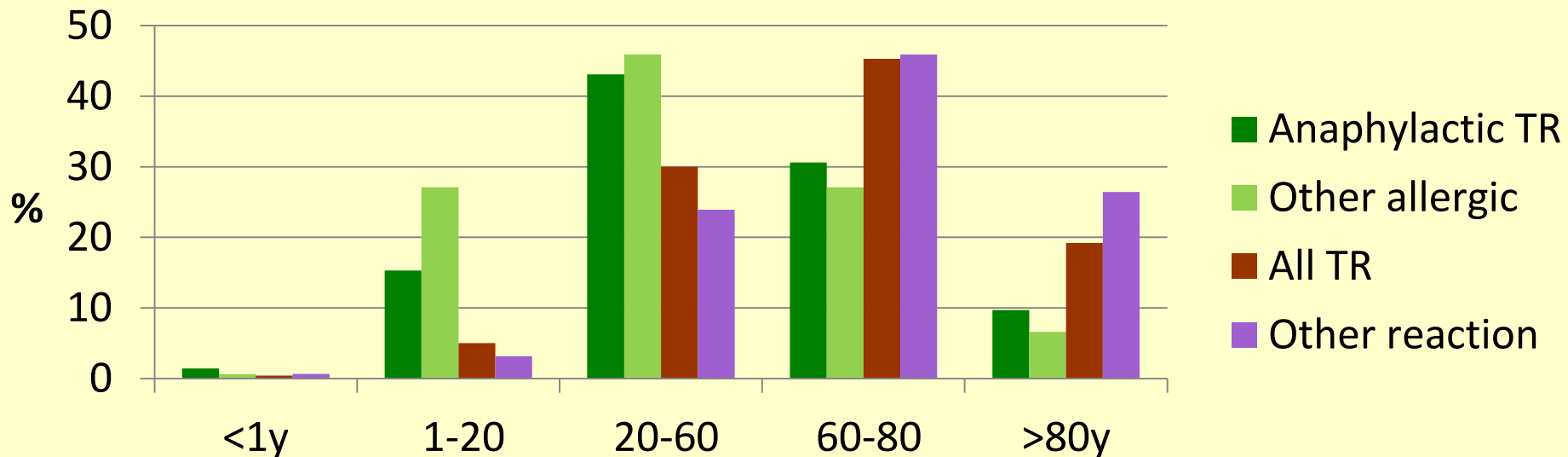
Type of blood component



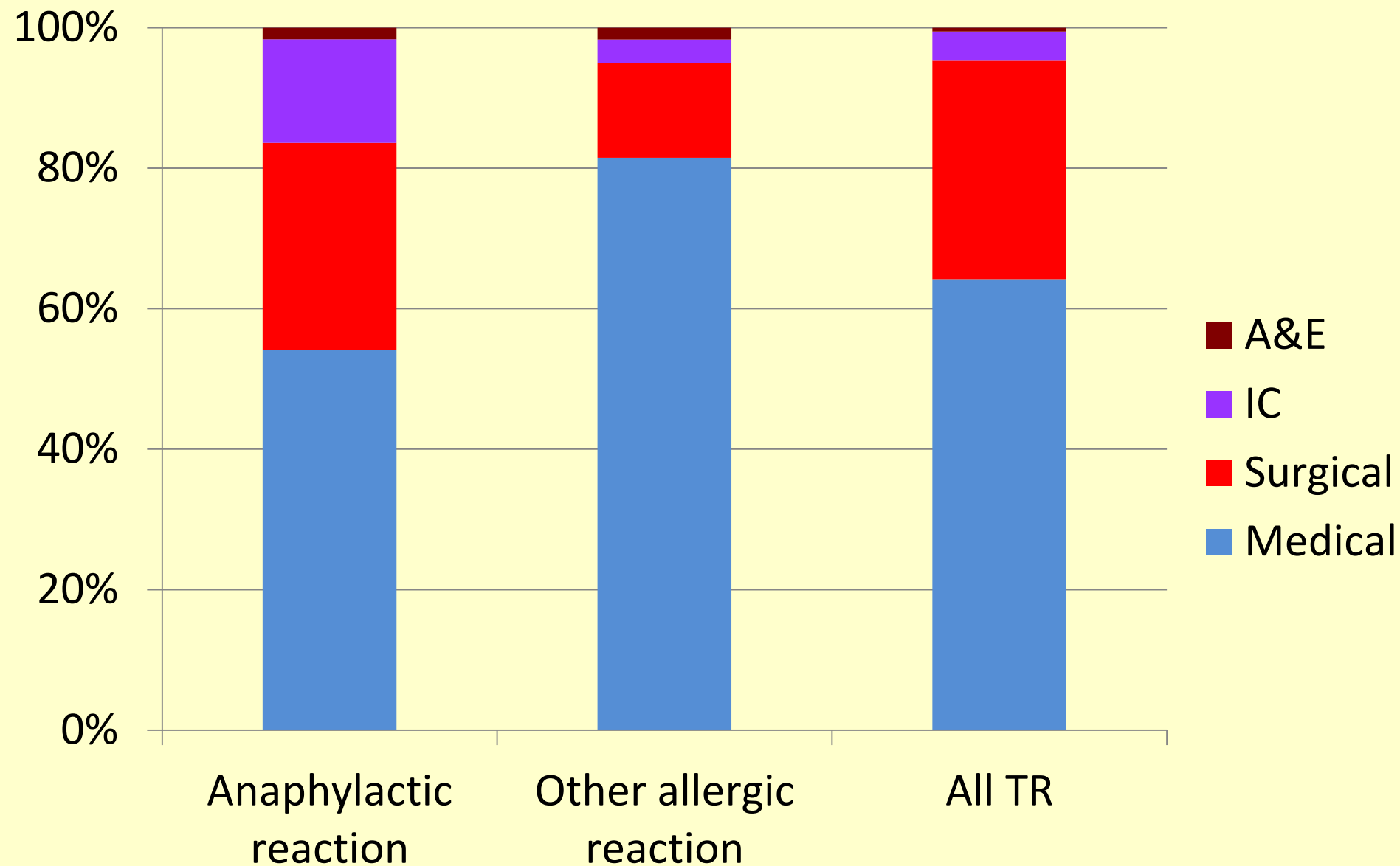
Allergic and anaphylactic TR 2008-2010 by hospital annual blood use



Age of recipients



Specialty



2008-2011 6 patients with 2 serious anaphylactic reactions or 1 anaphylactic + 1 other reaction or TACO

- 3m, 3f
- Age 17-91
- MDS (3x), lymphoma (2x) familial HUS / therapeutic plasmapheresis

2010-2011 further 5 patients with multiple (2-4) allergic/allergic reactions

- 1m, 4f
- Age 8-52
- Rejection of transplanted kidney, leukemia (3x), TTP

Platelets > plasma > RBC



TRIP database

2008-2011 6 patients with 2 serious anaphylactic reactions or 1 anaphylactic + 1 other reaction or TACO

- 3m, 3f
- Age 17-91
- MDS (3x), lymphoma (2x) familial HUS / therapeutic plasmapheresis

2010-2011 further 5 patients with multiple (2-4) allergic/allergic reactions

- 1m, 4f
- Age 8-52
- Rejection of transplanted kidney, leukemia (3x), TTP

Platelets > plasma > RBC

2010-2011 further 7 patients with multiple (2-4) other reactions

- 2m, 5f
- Age 15-84

(Serious) allergic reaction recommendations

CBO Revised transfusion guideline (2011):

1. **IgA level** and **anti-IgA** determination (and IgA subtype if this deficiency is suspected)
2. If repeated serious allergic/anaphylactic reactions occur or if anti-IgA is found use washed RBC/platelets; plasma from IgA deficient donors.
3. For other allergic reactions, give antihistamine and continue transfusion under careful observation; consider prophylactic antihistamine next time.

Looking for a cause

Allergic and anaphylactic reactions 2002-2011
Total N=2185

Anti-IgA

103 reports state normal IgA result and/or absence of anti-IgA

4 reports of documented IgA deficiency + anti IgA

Population estimated 1 in 600 deficient

Other specific cause?

1 report (suggestive) patient peanut allergy

NEJM 2011;364:1981-2

ABO incompatibility of platelets?

Anaphylactic and other allergic reactions,
2008-2011 with platelets (N=487)

97 No information

298 ABO identical

75 ABO compatible

(patient has no antibodies against donor ABO)

17 ABO incompatible

(patient has antibodies against donor ABO)

CBO transfusion guideline:

As far as possible, give ABO identical platelets

Other investigations

Anaphylactic and other allergic reactions,
2008-2011 (N=1000)

HLA-antibodies

10 Platelets: refractoriness + HLA investigated

16 HLA-ab detected or known to be present

68 HLA-ab determined, negative

*Role ~ platelet refractoriness

Male-only Q FFP from mid 2007

Male-only plasma for platelet pools Nov 2009

Anaphylactic	2007		2008		2009		2010		2011	
	>Gr1	all	>Gr1	all	>Gr1	all	>Gr1	all	>Gr1	all
RBCs	2	10	7	14	4	12	4	18	3	15
Platelets	9	26	14	30	7	31	10	37	7	26
FFP	8	12	5	15	8	23	3	13	8	17
Platelets RBCs and/or plasma	2	4	4	4	0	3	1	2	1	4
RBCs + plasma	1	1	0	2	0	0	0	1	1	2
Total	22	54¹	30	65	21²	71²	19²	72³	21²	66²

¹ product type not specified in one report

² two reports, one serious, involved the administration of unwashed autologous drain blood

³ one serious report involved the administration of unwashed autologous drain blood



Serious transfusion reactions

Transfusion reactions	2003	2004	2005	2006	2007	2008	2009	2010	2011	Total
AHTR	4	7	8	6	2	7	6	6	8	54
Anaphylactic	4	11	20	12	21	29	20	18	20	155
Other allergic	3	10	7	9	2	5			3	39
Hemosiderosis				3	3	2		1	2	11
Mild NHFR	2	3	1		3	3	4	4	2	22
NHTR	4	11	10	20	17	21	15	6	7	111
new allo-ab	1	3				3	2	1		10
Other reaction	4	12	4	2	5	11	15	17	21	92
Post-tf bacteremia	2	1	5	3	3	3	1	4	3	25
Post-tf other infection									1	1
PTP									2	2
Post-tf viral infection	1	1	1	2	2	1	0	0	1	9
TRALI	3	5	12	18	25	18	13	12	5	111
Delayed HTR	2	5	2	8	4	4	3	5	1	34
TACO	1	4	9	22	14	17	15	17	18	117

TRIP reports

- 2004** Important categories such as **anaphylaxis**, non-hemolytic transfusion reactions and new allo-antibodies should be the subject of further study. It is important to **learn how to identify at-risk patients**.
- 2005** **Anaphylactic reactions** are an important type of **serious** reports. They are relatively often caused by fresh frozen plasma or platelet concentrates. There is a **lack of knowledge of possible preventive (product) measures**.
- 2006** Recommendation 1 from the TRIP Report 2005 remains relevant: Research is needed into the causes of **anaphylactic transfusion reactions**. Subsequently one needs to search for blood **components that cause fewer** anaphylactic reactions and to investigate these components in comparative clinical studies.'
- 2009** **Anaphylactic reaction** is now the largest category of serious transfusion reaction.
- 2010** A **standard protocol** should be developed for the further investigation of **serious anaphylactic** transfusion reactions.
Action: TRIP and Sanquin Clinical Advisory Service

- Transparency, trends, benchmarking
- Generating signals
- Picking up rare events
- Highlighting areas for further research

BUT

- Reporting bias, under-reporting
- Limited denominator data
- Lack of information on confounders

Allergic and anaphylactic TR, 2009-2010

Platelet type	Reports	Units distributed nationally
Apheresis	9%	9%
Pooled, PAS	10%	19%
Pooled, plasma	60%	71%
Irradiated (total)	47%	35%
Component type not specified	21%	

Per 100.000	SHOT (UK) 2010	France 2010	NL 2010	Johns Hopkins
NHTR (febrile)				
Platelets	11.7	71	120	
RBC	11.4	59	74	
Plasma	1.1	1.3	8	
Allergic				Savage et al Transfusion 2011;51:1716- 1722
Platelets	23.9	280 66 Pool 461 Apheresis	219	1723 Aph P = 1.7%
RBC	3.4	13.6	10	
Plasma	10.8 (20% SD distr)	50 Serious: 17 FFP 3.9 SD 9.6 MB	77	

Where next?

- Improve registration
 - Patient's diagnosis; reason for Tf
 - Specific component type
 - Blood group of product(s) and patients
- Analyses limited: observational system
 - Need to collaborate!
- Future developments
 - ?age of product
 - Serious allergic TR: develop protocol for joint analysis with Sanquin
 - Post-marketing surveillance to monitor effect of component modification

Acknowledgements

- **TRIP** colleagues
- **TRIP** contact people

