FROSTED study

FResh frozen plasma,
Omniplasma &
SDP comparison of
Transfusion reactions,
Efficacy &
DVT

Transfusie-gerelateerde longschade (TRALI) en andere bijwerkingen bij plasma transfusies – een samenvatting

Plasma transfusion are indicated in the following cases:

Clinical condition	GoR
1. Correction of congenital or acquired deficiencies of clotting factors (for which there is not a specific concentrate), when the PT or aPTT ratio is >1.5:	
- Liver disease:	
- *active bleeding*	1C+
- *prevention of bleeding in the case of surgery or invasive procedures*	2C
- During treatment with vitamin K antagonists (if prothrombin complex, which is the first choice treatment, is not available):	1C+
- *in the presence of major or intracranial haemorrhage*	
- *in preparation for surgery than cannot be delayed*	
- Acute disseminated intravascular coagulation with active bleeding, in association with correction of the underlying cause	1C+
- Microvascular bleeding during massive transfusions (>1 blood volume), even before the results of PT and aPTT	1C+
- Deficiencies of single clotting factors, in the absence of specific concentrates (e.g. of FV), in the presence of active bleeding or to prevent bleeding during an invasive procedure	1C+
2. Apheretic treatment of thrombotic microangiopathies (thrombotic thrombocytopenic purpura, haemolytic-uraemic syndrome, HELLP syndrome), as a replacement fluid	1A
3. Reconstitution of whole blood for exchange transfusions	2C
4. Hereditary angioedema in the case that C1-esterase inhibitor is not available	2C+

Legend: GoR: Grade of recommendation; HELLP: haemolytic anaemia elevated liver enzymes and low platelet count

Liumbruno, G., Bennardello, F., Lattanzio, A., Piccoli, P., & Rossetti, G. (2009). Recommendations for the transfusion of plasma and platelets. Blood Transfusion, 7(2), 132–50.

Plasma transfusies – clinical practice:

Procedure/clinical indication	Percentage of FFP transfusions
Surgery	33.3%
Warfarine reversal	20.2%
Other coagulopathies	14.3%
Prior to invasive surgery	5.9%
Bleeding	8.4%
Massive transfusion	7.3%
Plasmapheresis	3.8%
Trauma	0.3%
Other	6.3%

"55% of plasma transfusions could be qualified as appropriate based on internationally agreed-upon indications, with fully 28% qualifying as inappropriate and the remainder as indeterminate"

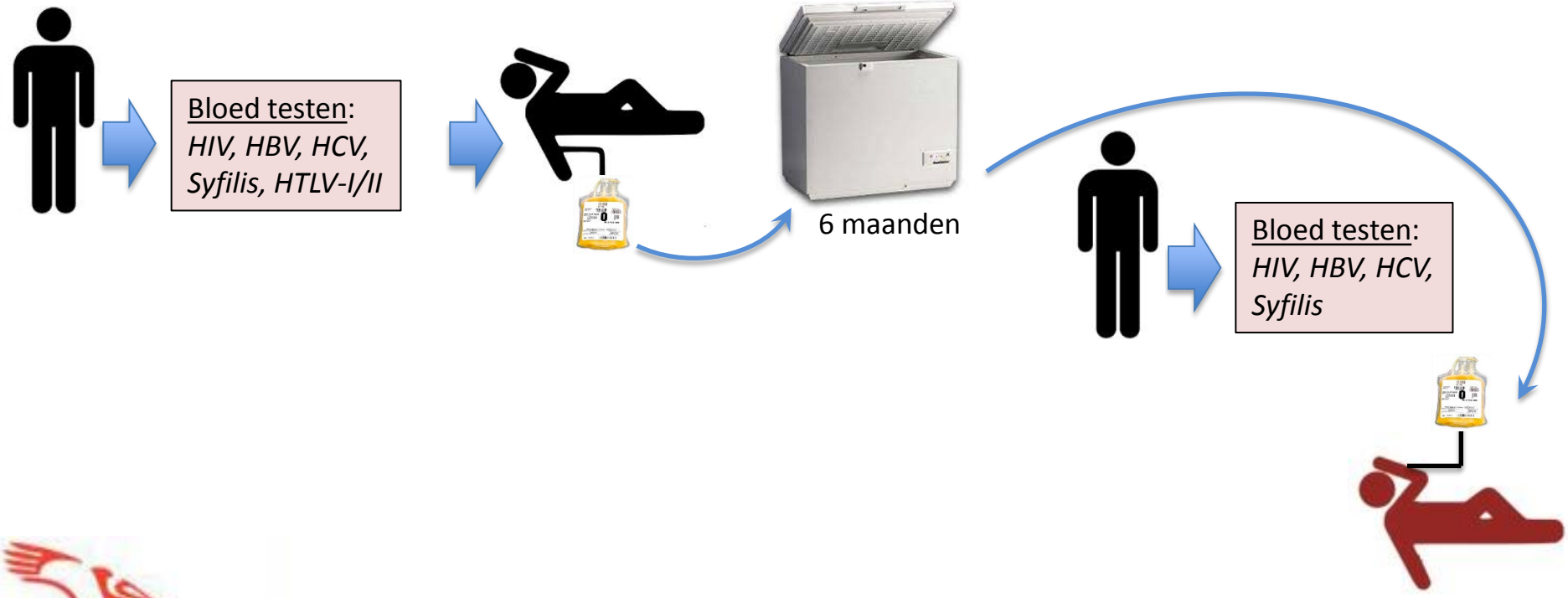
Plasma transfusions – possible adverse events:

- Allergic/anaphylactic reaction
- Febrile Non-Hemolytic Transfusion Reaction (FNHTRs)
- Acute hemolytic transfusion reaction (via RBC alloimmunization)
- Bacterial transfusion reaction
- Transfusion Related Acute Lung Injury (TRALI)
- Transfusion Associated Circulatory Overload (TACO)
- Venous thrombo-embolism (DVT, PE)
- Hyperfibrinolysis

Plasma types:

Quarantined Fresh Frozen Plasma (Q-FFP)

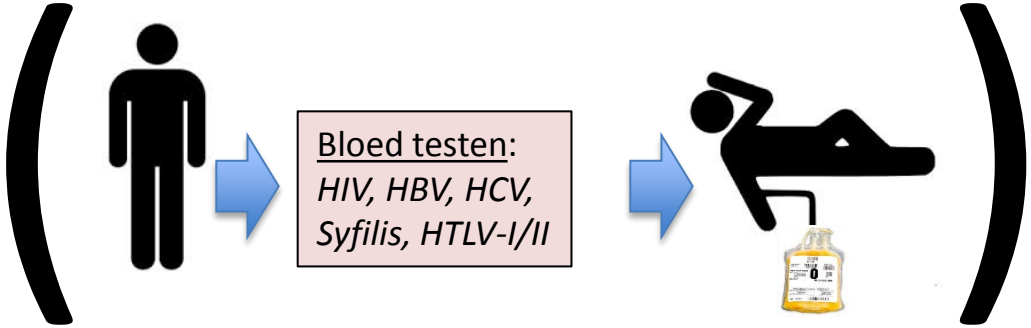
- Aferese plasma (van één donor) in quarantaine voor zes maanden
- Donor getest op bepaalde ziekten
- Hertesten na zes maanden (window period)
- Plasma gebruikt als donor twee testen haalt
- Verloopt: 24 maanden na donatie

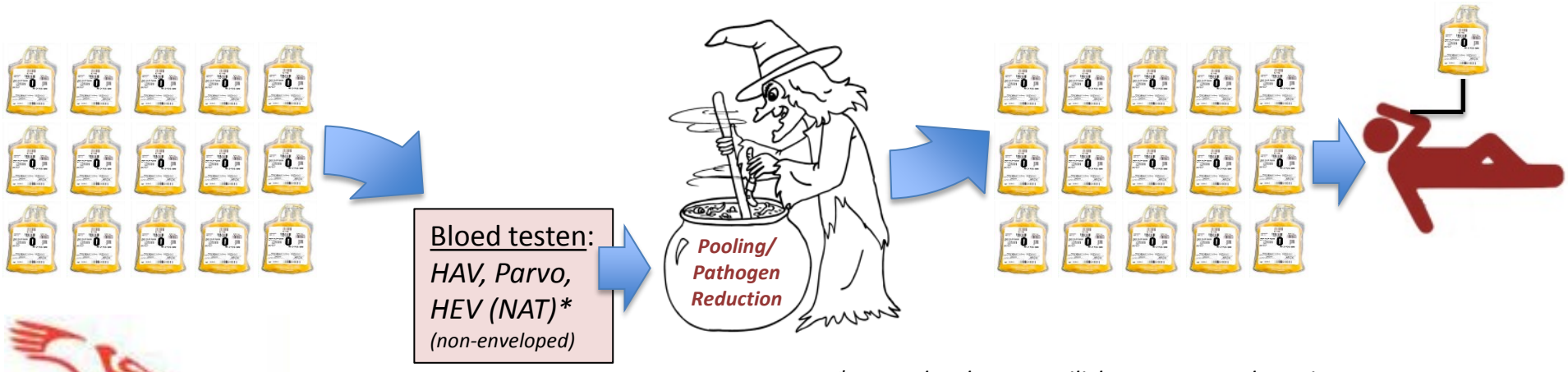


Plasma types:

Solvent/Detergent treated pooled Plasma (SDP) – e.g. Omniplasma™

- Plasma van ~1000 donoren gepoold
- Pathogeen reductie proces op pool
- Plasma gedeeld in eenheden





*Testen levels van antilichamen tegen deze virussen

Research question:

What are the internationally reported incidences of adverse events to plasma transfusions?

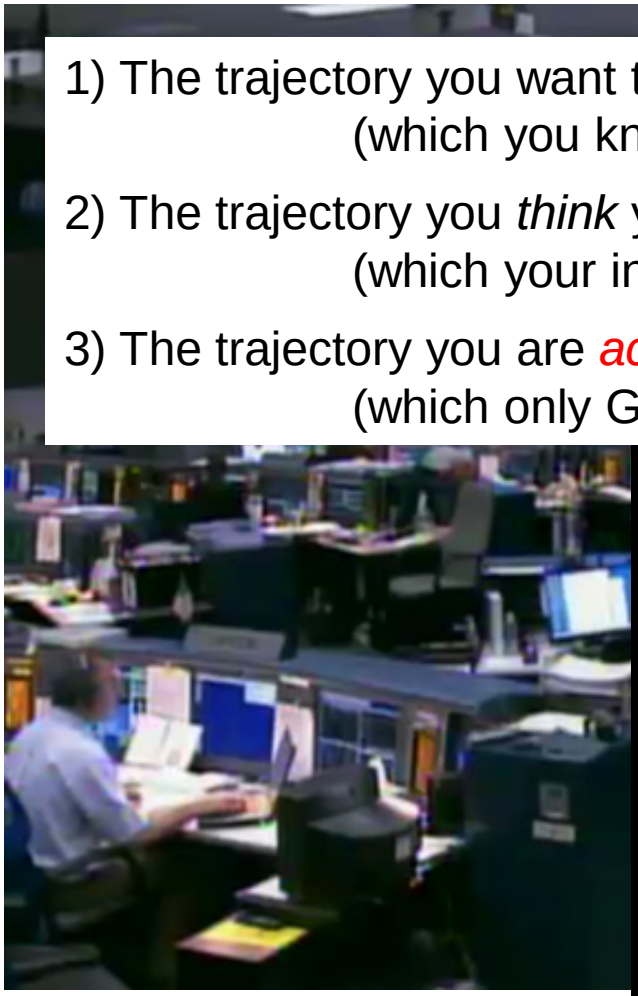
This page contains proprietary data and is thus excluded from this version of the presentation

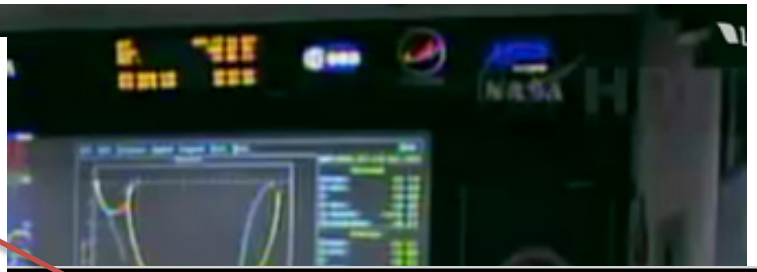
The story of the three trajectories…

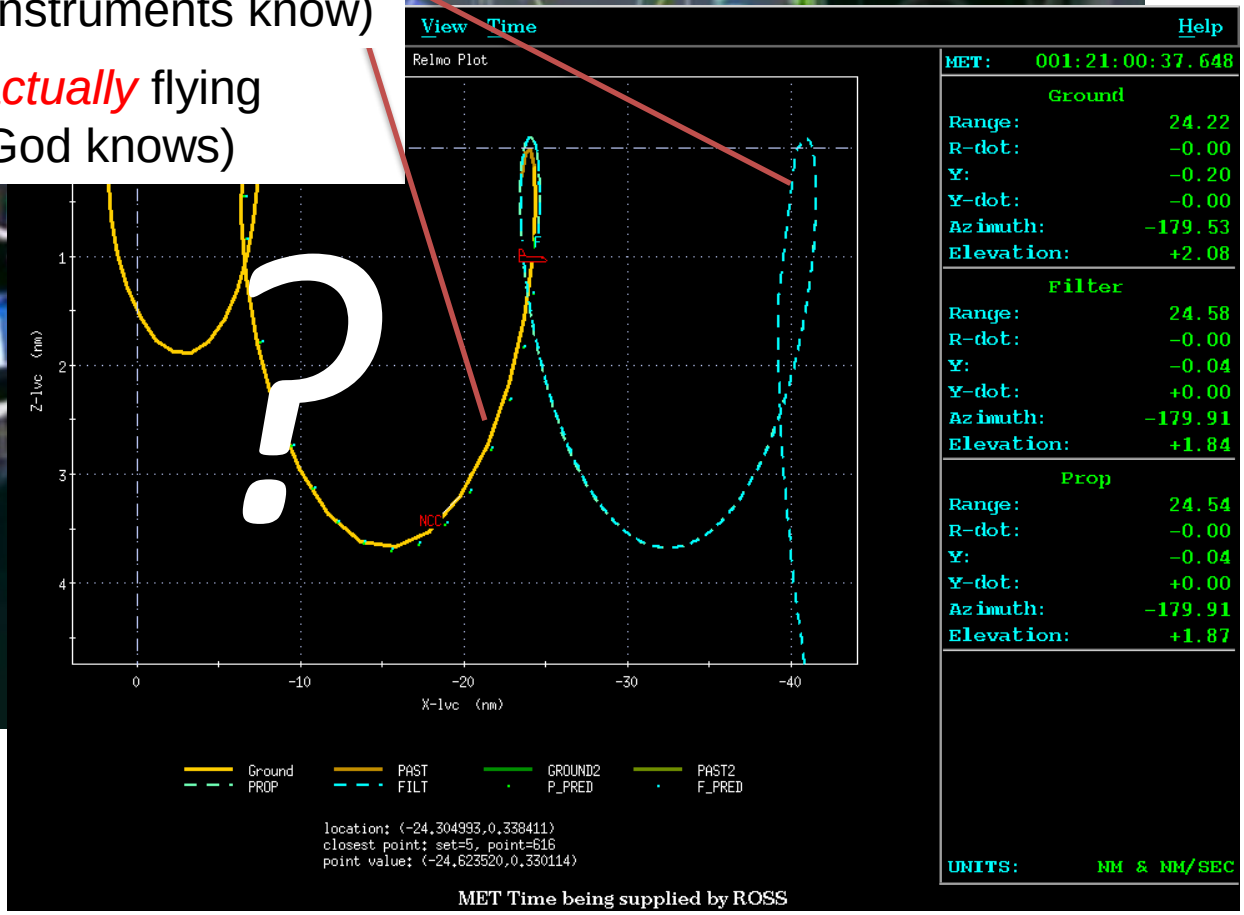
1) The trajectory you want to fly
(which you know)

2) The trajectory you *think* you are flying
(which your instruments know)

3) The trajectory you are *actually* flying
(which only God knows)







This page contains proprietary data and is thus excluded from this version of the presentation

This page contains proprietary data and is thus excluded from this version of the presentation

This page contains proprietary data and is thus excluded from this version of the presentation

Discussion:

- Three effects at play here?
  - Random error
  - Observation bias?
  - Inconsistent definitions

Discussion:

- Three effects at play here?
  - Random error
  - Observation bias?
  - Inconsistent definitions

- Random error
  - Small studies tend to yield either a null incidence or a very high incidence

The figures on this page contain proprietary data and are thus excluded from this version of the presentation

Discussion:

- Three effects at play here?
  - Random error
  - Observation bias?
  - Inconsistent definitions

- Observation bias?
  - Odaka et al. (2012)

    ~56000 units FFP transfused

    509 allergic reactions

    ~100 allergic reactions per 10e5 transfusions

    ~18x higher incidence than large studies

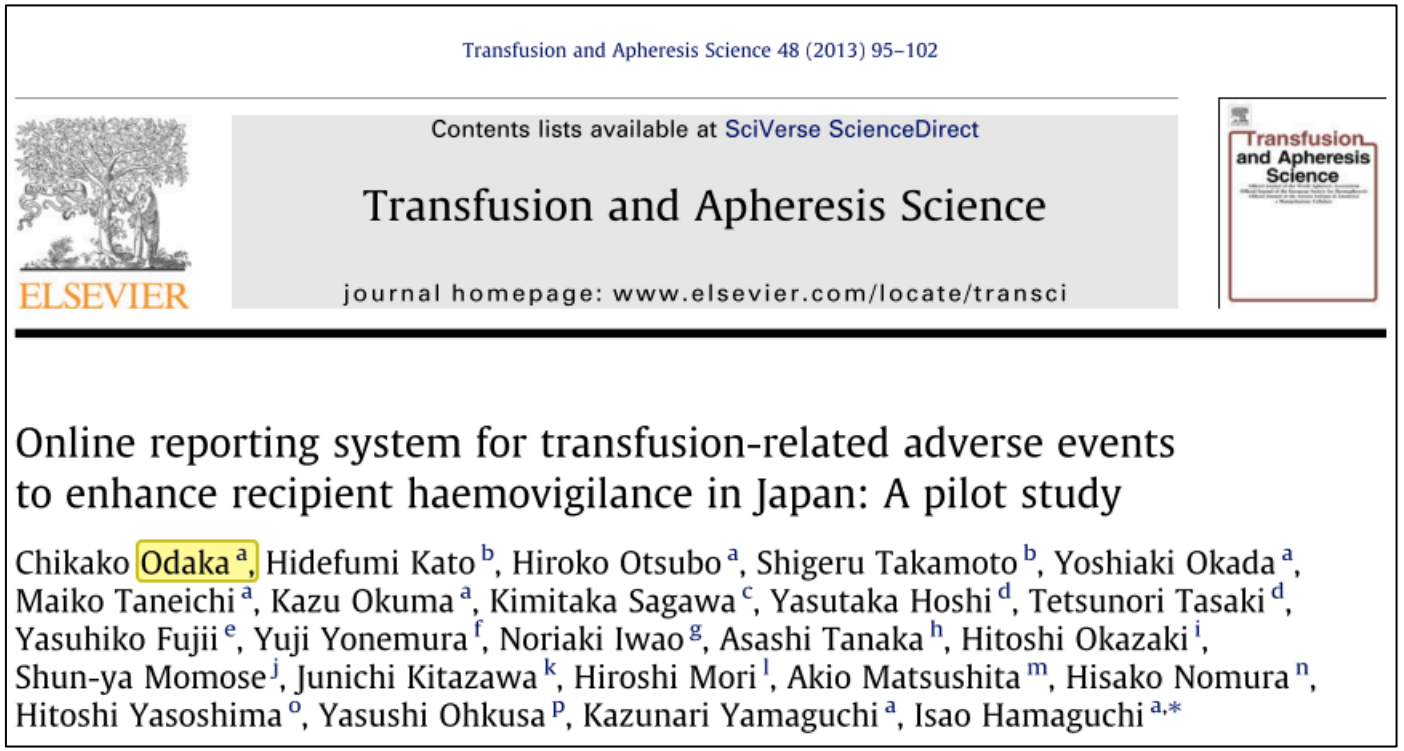
The figures on this page contain proprietary data and are thus excluded from this version of the presentation

This page contains proprietary data and is thus excluded from this version of the presentation

This page contains proprietary data and is thus excluded from this version of the presentation

Observation bias (cont'd)

- Odaka et al. (2012)
  - ~56000 units FFP transfused
  - 509 allergic reactions
  - ~100 allergic reactions per 10e5 transfusions
  - *~18x higher incidence than large studies*



Transfusion and Apheresis Science 48 (2013) 95–102

Contents lists available at SciVerse ScienceDirect

Transfusion and Apheresis Science

journal homepage: www.elsevier.com/locate/transci

Online reporting system for transfusion-related adverse events to enhance recipient haemovigilance in Japan: A pilot study

Chikako Odaka [a], Hidefumi Kato [b], Hiroko Otsubo [a], Shigeru Takamoto [b], Yoshiaki Okada [a], Maiko Taneichi [a], Kazu Okuma [a], Kimitaka Sagawa [c], Yasutaka Hoshi [d], Tetsunori Tasaki [d], Yasuhiko Fujii [e], Yuji Yonemura [f], Noriaki Iwao [g], Asashi Tanaka [h], Hitoshi Okazaki [i], Shun-ya Momose [j], Junichi Kitazawa [k], Hiroshi Mori [l], Akio Matsushita [m], Hisako Nomura [n], Hitoshi Yasoshima [o], Yasushi Ohkusa [p], Kazunari Yamaguchi [a], Isao Hamaguchi [a,*]

Observation bias (cont'd)

- Odaka et al. (2012)
  - ~56000 units FFP transfused
  - 509 allergic reactions
  - ~100 allergic reactions per 10e5 transfusions
  - *~18x higher incidence than large studies*

Clinical signs	RBC	PC (Number of cases)	FFP
1) Fever			
2) Chill・Rigor			
3) Feverishness			
4) Pruritus			
5) Rash			
6) Urticaria			
7) Respiratory distress			
8) Nausea・Vomiting			
9) Headache			
10) Chest, flank or back pain			
11) Hypotension			
12) Hypertension			
13) Tachycardia			
14) Vein pain			
15) Disturbance of consciousness			
16) Hemoglobinuria			
17) Others			
17) Others			

Observation bias (cont'd)

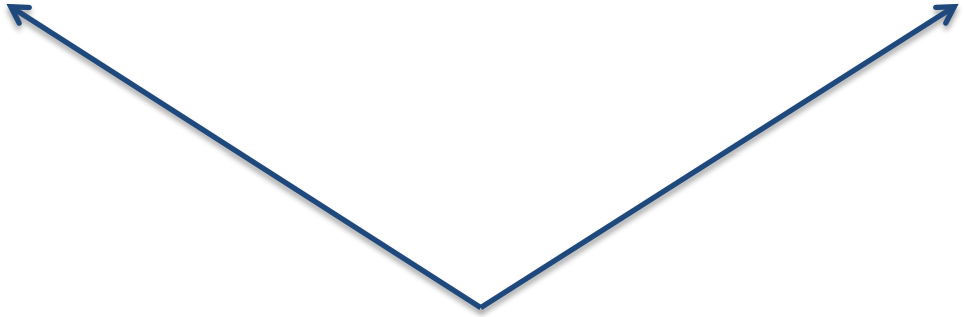
- Odaka et al. (2012)
  - ~56000 units FFP transfused
  - 7 anaphylactic reactions
  - ~1 anaphylactic rxn per 10e5 transfusions
  - *~7x higher incidence than large studies*

The figures on this page contain proprietary data and are thus excluded from this version of the presentation

Observation bias (cont'd)

- Odaka et al. (2012)
  - ~56000 units FFP transfused
  - 509 allergic reactions
  - ~100 allergic rxns per 10e5 transfusions
  - *~18x higher incidence than large studies*

  7 anaphylactic reactions
  ~1 anaphylactic rxns per 10^e5 transfusions
  ~7x higher incidence than large studies



Anaphylactic reactions offer more overt symptoms and are therefore less subject to observer bias…

…so what do Odaka et al. have to say about TRALI?

This page contains proprietary data and is thus excluded from this version of the presentation

Discussion:

- Three effects at play here?
  - Random error
  - Observation bias?
  - Inconsistent definitions

- Inconsistent definitions
  - Despite the IHS' insistence, many countries do not abide to the agreed-upon definitions/thresholds for the various adverse events
  - Differing definitions yield inconsistent reported incidences
  - Differing definitions yield data sets *not amenable to comparison*

Why do we need consistent definitions of adverse events?

- Transfusion reaction pathophysiology is not yet well understood
- The power of an epidemiological approach to uncovering the underlying mechanisms, and thus produce viable treatment options, is hindered by the lack thereof.
- Believe it or not, these sorts of discussions save lives….

Year	***No. TR related deaths (the Netherlands)***
2008	4
2009	3
2010	9
2011	6
2012	6

Bedankt:

- J.G. van der Bom (Anske) – LUMC, Sanquin
- M. Schipperus (Martin) – Hagaziekenhuis, TRIP
- R. Zoethout (Ruud) – Sanquin
- C. Kramer (Christine) – Sanquin
- Medewerkende ziekenhuizen (LUMC, Albert Schweitzer, Haga,…)

Dank u vriendelijk