Storage medium and transfusion transmitted bacterial infections

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Bloed is leven

TRANSFUSION

BLOOD COMPONENTS

Storage medium of platelet transfusions and the risk of transfusion-transmitted bacterial infections

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The Dutch situation

- Buffy coats after overnight hold
- 5 donors

- Apheresis products for specific indications

- PAS (25ml plasma per donor) or plasma
  - Up to 2013: PAS-B (T-sol, Baxter)
  - 1-1-2013: PAS-C (Intersol, Fenwal, inc)

- Geographic location of the hospital

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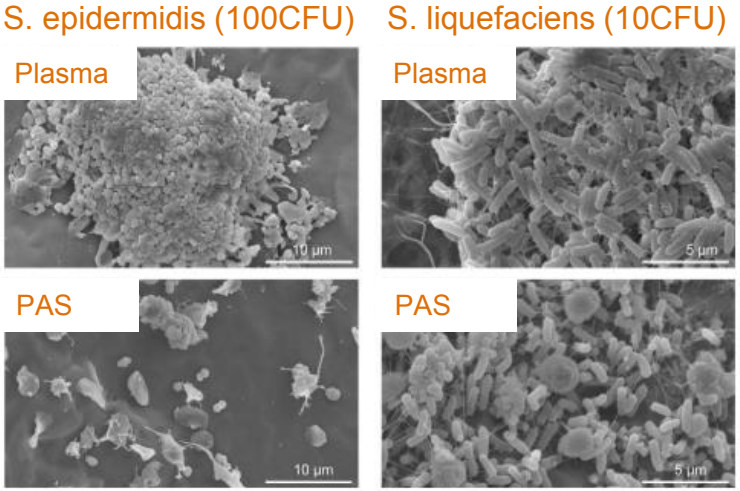
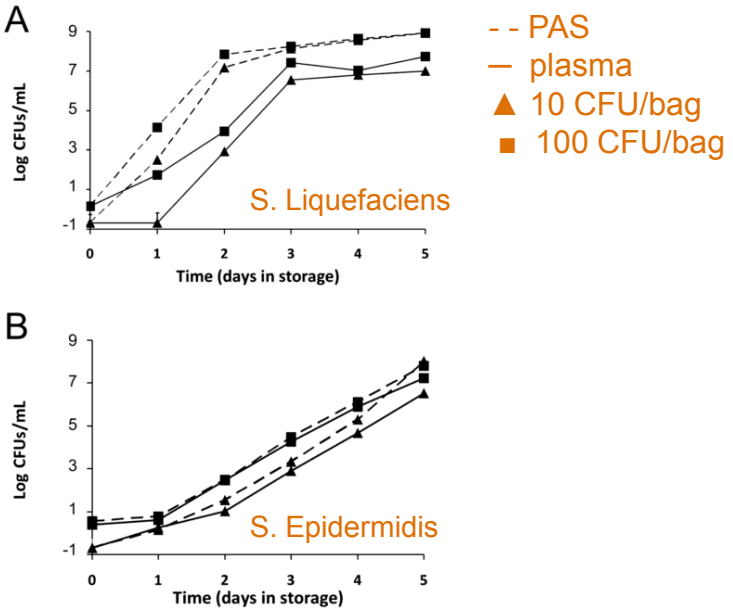
The Dutch situation

PAS or plasma → Does it matter?

In vitro – Greco et al.



Scanning electron micrograph inner surface PLT bag



- PAS-E:
  - Reduced biofilm formation by S. liquefaciens and S. epidermidis
  - Earlier detection of S. liquefaciens by colony counting

Greco et al. Transfusion 2010; 50(11): 2344-2

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In vitro – Dumont et al.

- PAS-C
  - 5 bacterial strains
  - More rapid initiation of log-phase growth
  - 4 logs higher bacterial concentration after 24 hours
  - No difference in concentration max

TABLE 4. Storage medium effects

Growth variable	Estimated difference*	SE†	95% CI	p value
Doubling time (hr)	0.14	0.05	0.03 to 0.25	0.023
Lag time (hr)	4.7	1.5	1.2 to 8.2	0.016
Conc-max ($\times 10^8$ CFUs/mL)	−1.0	0.7	−2.7 to 0.8	0.222
Time-max (hr)	0.57	4.4	−9.9 to 11.1	0.902

* The difference plasma minus PAS.
† SE = standard error of the estimated difference.

Dumont et al. Transfusion 2011;51:1079-1085.

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PAS or plasma – Aim

- Differences in growth characteristics
  → difference in screening?
  → clinical consequences?

- Aim:
  To quantify the association of storage medium with the incidence of TTBI after transfusion of a PLT concentrate

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Bacterial screening

- Aeroob and anaeroob bottle, inoculated 7,5ml each
- BacT/Alert (bioMérieux)
- Negative to date policy
- Maximal storage time 7 days

- Universal skin disinfection method
- July 2004: diversion pouch

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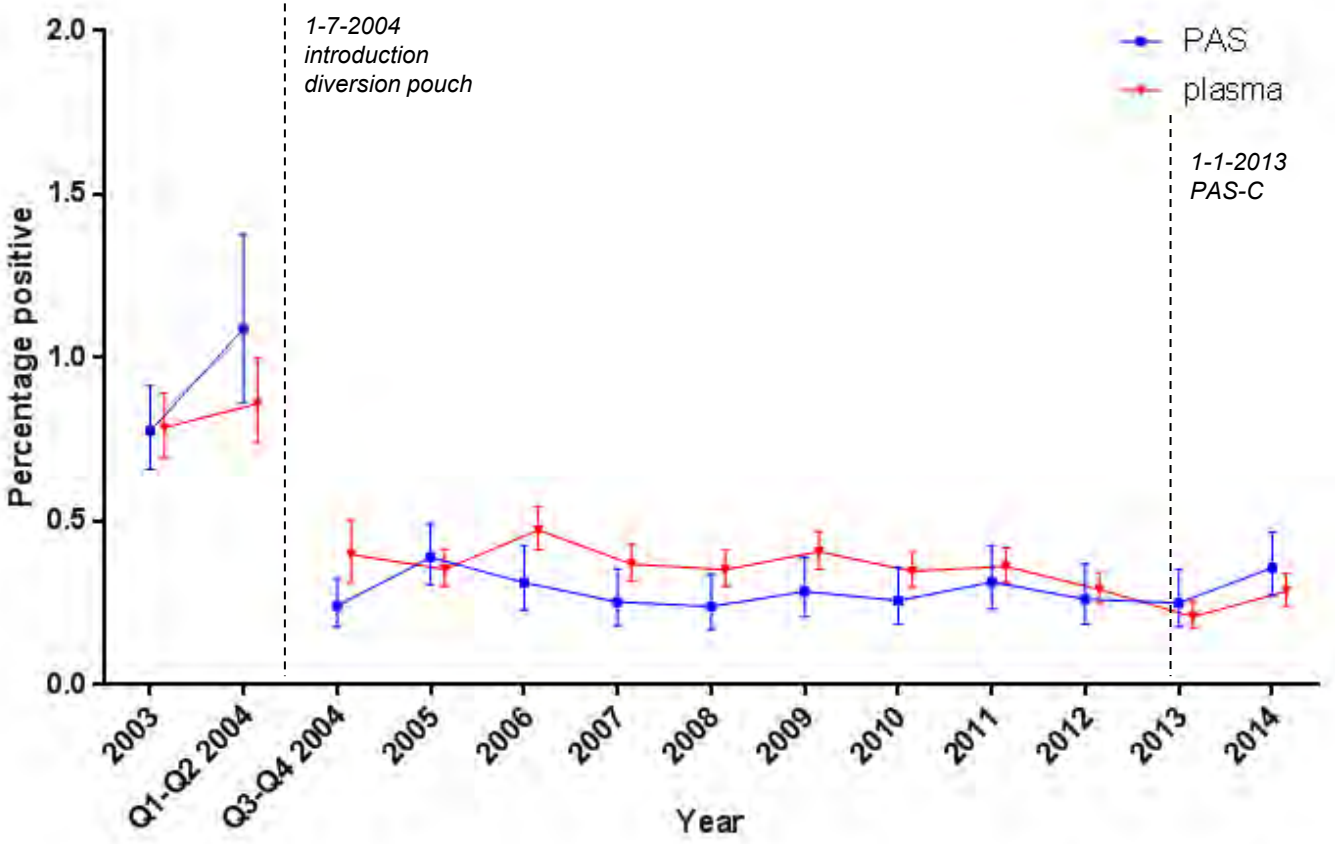
Bacterial screening: results



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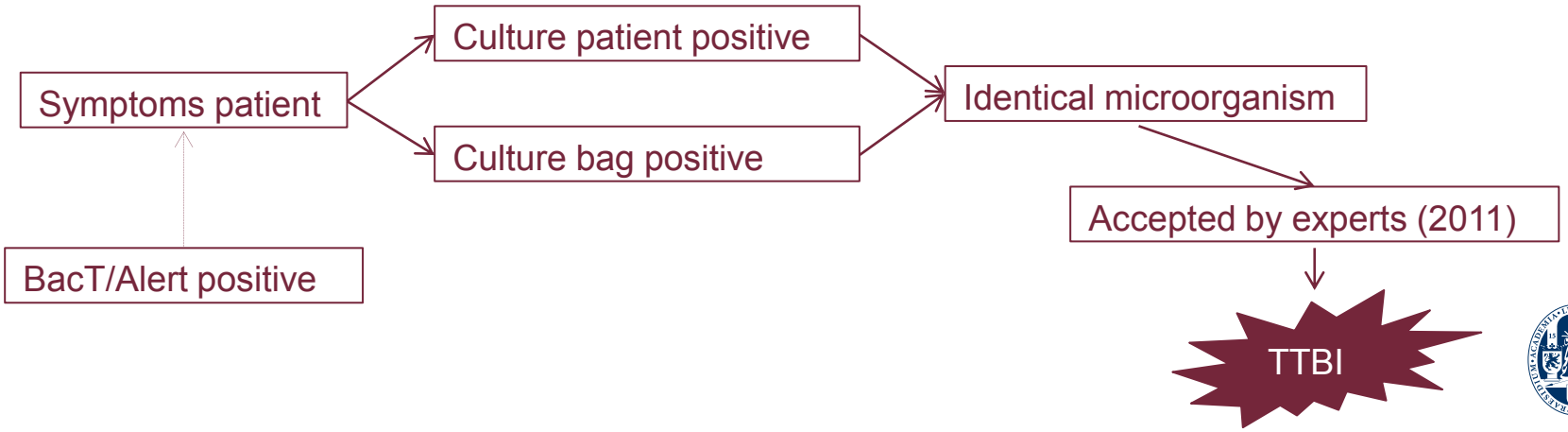
TRIP

- Transfusion and transplantation Reactions In Patients
- Dutch competent authority
- 2003-2014

TRIP Hemo- en biovigilantie

- TTBI: Clinical features of bacteremia or sepsis during or after transfusion, with a relevant positive blood culture in the patient and assessed with a high level of imputability to the transfused product.



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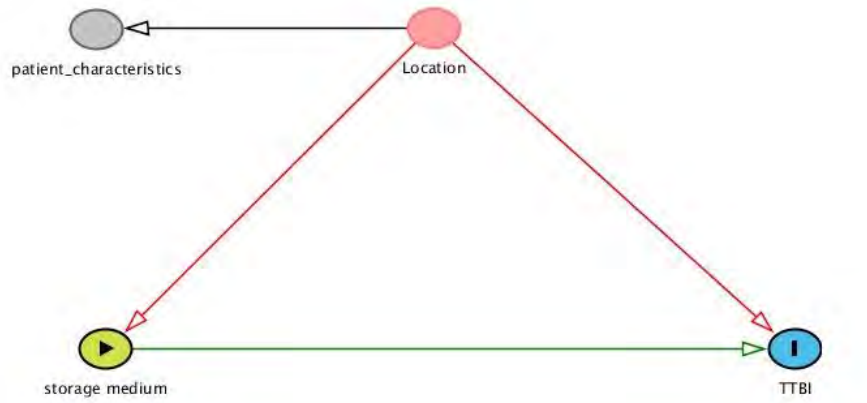
Methods

- Nested case control
- All cases of TTBI after PLT transfusion reported to TRIP
- Denominator: all produced PLT concentrates 2006-2014

- Location of hospital as instrumental variable
- Assumption: equal distribution of all potential confounders



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Transfusion-transmitted bacterial infections

Year	Age in years	Diagnosis	Severity*	Bacteria	Storage medium
2003	18	Acute myeloid leukemia	2	Bacillus Cereus	**PAS-B**
2003	57	Chronic myeloid leukemia	N/A†	Bacillus Cereus	**PAS-B**
2004	28	N/A†	2	Bacillus Cereus	**PAS-B**
2005	33	Acute myeloid leukemia	2	Hemolytic streptococci group G	**Plasma**
2005	58	Mantle cell lymphoma	2	Bacillus Cereus	**PAS-B**
2005	46	Aplastic anemia	3	Staphylococcus aureus	**PAS-B**
2005	58	Non Hodgkin lymphoma	2	Hemolytic streptococci group G	**Plasma**
2008	53	Acute myeloid leukemia	2	Coagulase negative staphylococci	**Plasma**
2010	72	Prostate carcinoma	1	Coagulase negative staphylococci	**PAS-B**
2010	39	Acute myeloid leukemia	2	Streptococcus dysgalactiae	**PAS-B**
2011	59	Acute myeloid leukemia	2	Salmonella group B	**Plasma**
2012	75	Non Hodgkin lymphoma	2	Hemolytic streptococci group C	**Plasma**
2013	62	Chronic lymphoid leukemia	2	Coagulase negative staphylococci	**PAS-C**
2014	60	Multiple myeloma	4	Staphylococcus aureus	**Plasma**

Incidences TTBI

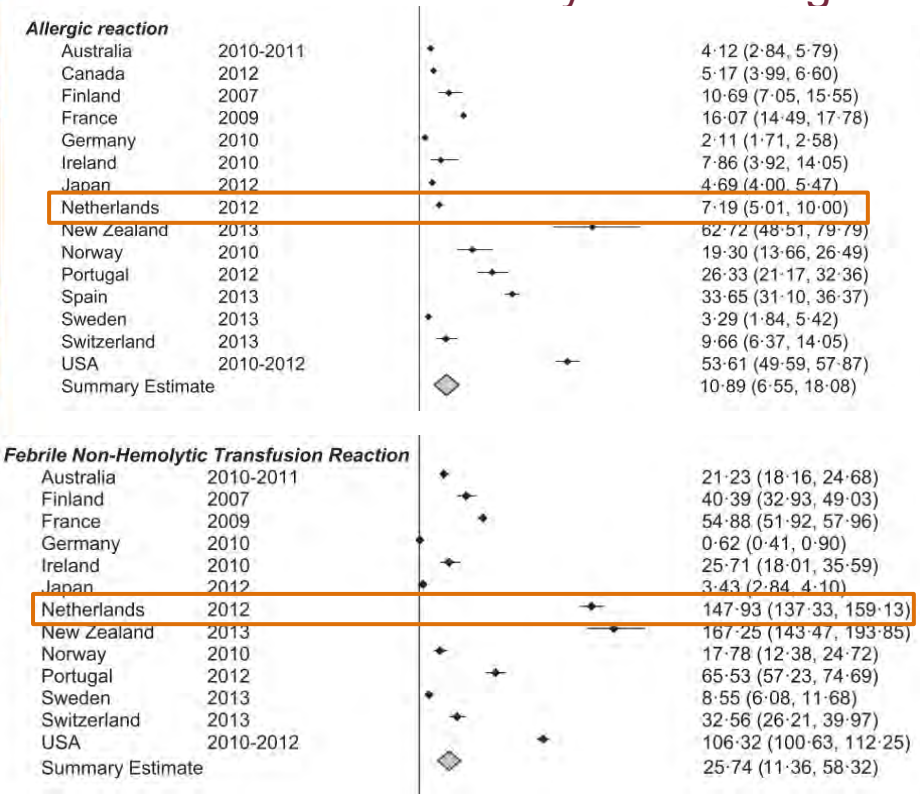
- Passive surveillance:
  - Without bacterial screening
    - France: 26.5/million PLT transfusions (2009-2011)
  - With bacterial screening
    - Germany: 7.14/million PLT transfusions (1997-2007)
    - USA: 9.35/million PLT transfusions (2007-2011)
    - UK: 0.56/million PLT transfusions (2009-2015)
- Active surveillance
  - Hong et al. 97.2/million PLT transfusions (2007-2013)
- Our study: 22/million PLT transfusions (2003-2014)

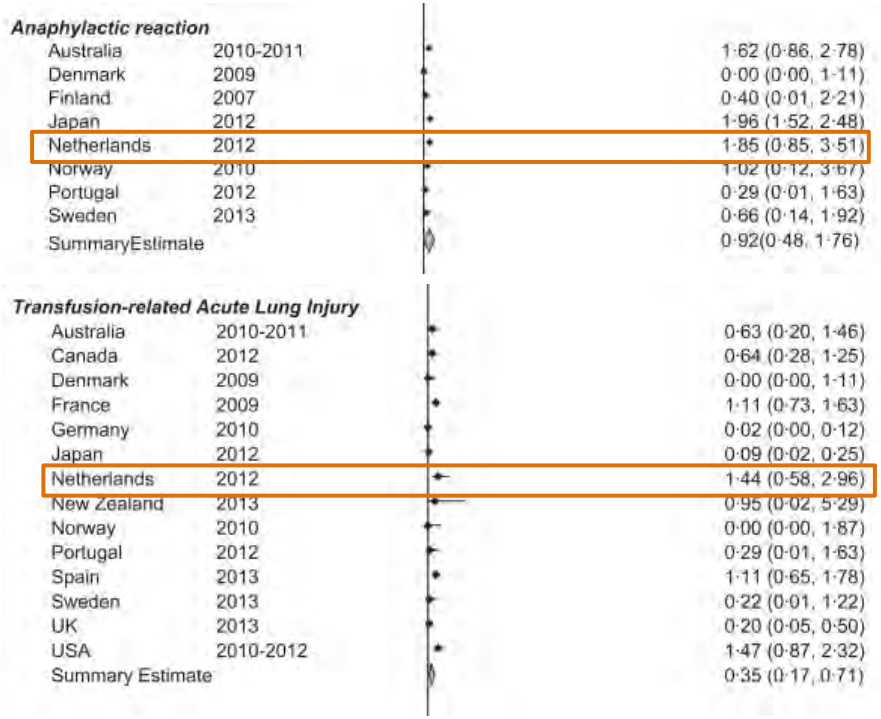
Keller-Stanislawski et al. Transfus Med 2009; 19: 340-349. Benjamin RJ et al. Vox Sang 2014; 106:23:30
SHOT annual report 2015. Daurat et al. Transfusion 2016; 56:1295-303. Hong, H. et al. Blood 2016: 127(4): 496-502

Incidences TTBI

- High incidence?

→ Accuracy of hemovigilance system



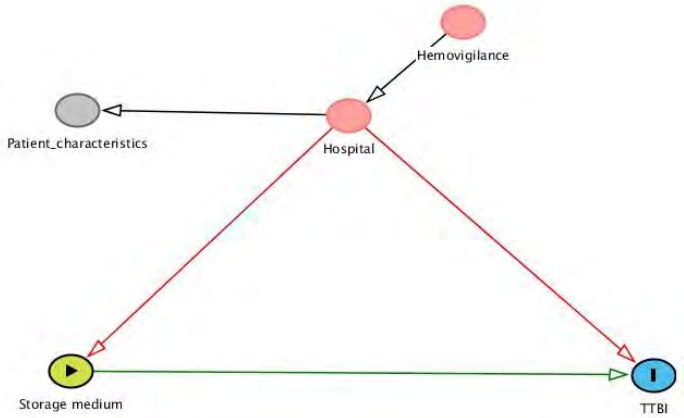


Rogers et al. Vox Sang 2016; 110:266-77

Main results

	TTBI - PLT	Sanquin
PAS	8 (57.1)	111 375 (22.3%)
Plasma	6 (42.9)	387 428 (77.7%)
OR		**4.63 (CI 1.4; 16.2)**

- Increased risk of TTBI after transfusion of PAS-stored PLTs compared to plasma-stored PLTs
  - Effect of exclusion criteria?
  - Differences in patient characteristics?
  - Differences in hemovigilance?



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Selection criteria?

- Exclusion of apheresis products
  - Special indication, mostly plasma

	TTBI - PLT	Sanquin
PAS	9 (56.3)	113 445 (20.4%)
Plasma	7 (43.8)	442 206 (79.6%)
OR		**5.01 (CI 1.66; 15.83)**

	TTBI - PLT	*Sanquin*
PAS	*8 (57.1)*	*111 375 (22.3%)*
Plasma	*6 (42.9)*	*387 428 (77.7%)*
OR		***4.63 (CI 1.4; 16.2)***

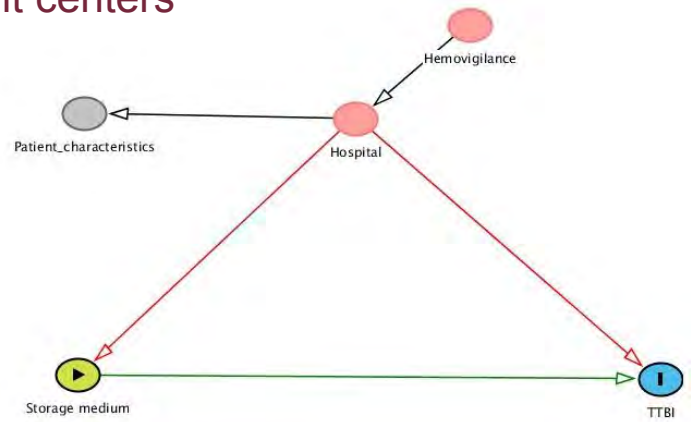
- Change in practice
  - Introduction of diversion pouch, exclusion all reactions before July 2004

	TTBI - PLT	Sanquin
PAS	6 (50.0)	111 375 (22.3%)
Plasma	6 (50.0)	387 434 (77.7%)
OR		**3.48 (CI 0.93; 13.01)**

Confounding?

- Assumption: equal distribution of all potential confounders
  - Patient characteristics: stem cell transplant centers

	SCT centers	Sanquin
PAS-hospital	20.4%	22.3%
Plasma-hospital	79.6%	77.7



  - Reporting behavior: RBC transfusion reactions

2013-2014	Sepsis	Sanquin
PAS-hospital	28 (28.3%)	198 333 (22.6%)
Plasma-hospital	71 (71.7%)	678 024 (77.4%)
OR		**1.34 (CI 0.87-2.09)**

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Conclusion

- Increased risk of TTBI after transfusion of PAS-stored PLTs compared to plasma
  - No differences in reporting behavior neither in patient characteristics
  - However, produced at different blood banks

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- All hospitals reporting transfusion reactions to TRIP

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TRIP
Hemo- en biovigilantie

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