NVB Nederlandse Vereniging voor Bloedtransfusie
PROFESSIONALS IN TRANSFUSIEGENEESKUNDE

NVB, 18 mei 2022

Scientific session, Ede

De rol van producteigenschappen (filtratie, bewaarduur) op de uitkomsten van transfusie

TRIM-research

Leo van de Watering, Afd. UTG Sanquin

TRIM?

Transfusion
Related
Immuno
Modulation

TRIM

- Alloimmunisatie
- Orgaan transplantatie
- Cancer recurrence
- Mortaliteit
- Infectie

Pre-TRIM

Pre-”TRIM”, voor 1970’s = RBC = Packed Cells +/- BC

1. **RBC transfusies kunnen anti HLA-Ab’s induceren**

2. **Anti HLA-Ab’s kunnen tot (acute) afstoting leiden**

➔ Aanname: Na RBC transfusie zullen patiënten slechtere transplantaat survival hebben

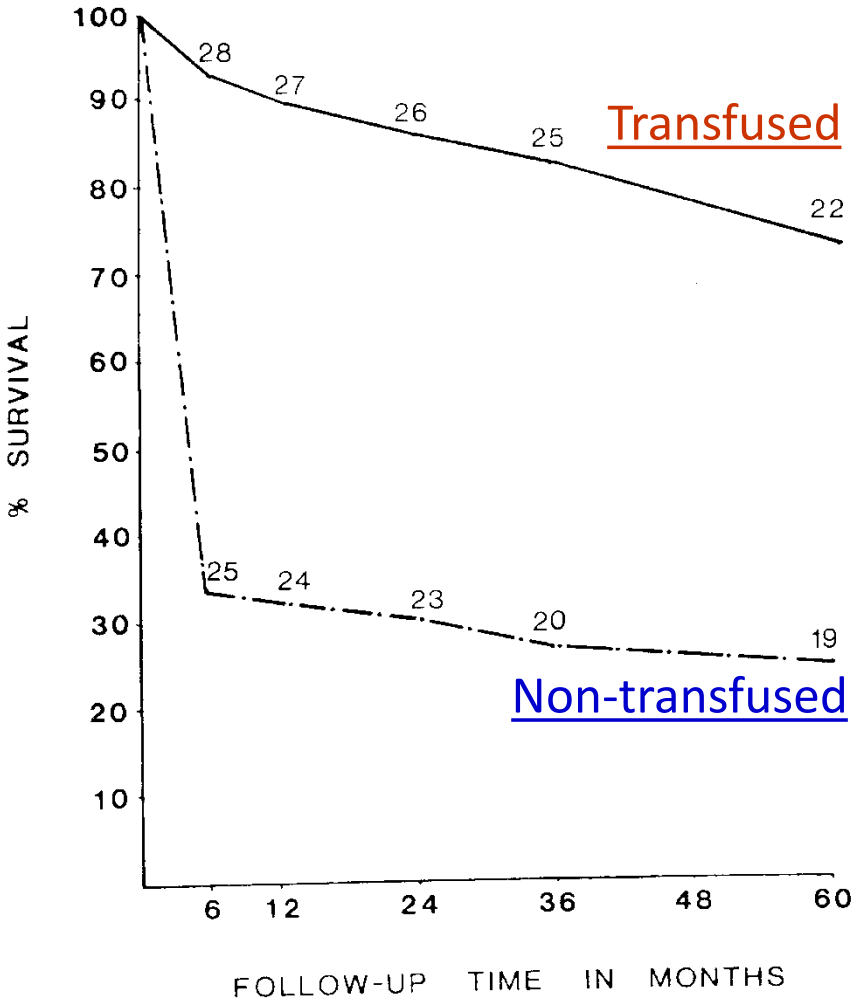


Figure 5.1. Kidney graft survival in the retrospective blood transfusion study. The ——— line represents the patients who have received 1 pretransplant blood transfusion while the non-transfused patients are represented by —.—. line. The overall difference is very significant ($p = 0.00001$).

G.G. Persijn, Thesis 1985

Opelz 1973

Kidney graft survival:
Pre-transplant transfused patients show better graft-survival than non-transfused.

TRIM

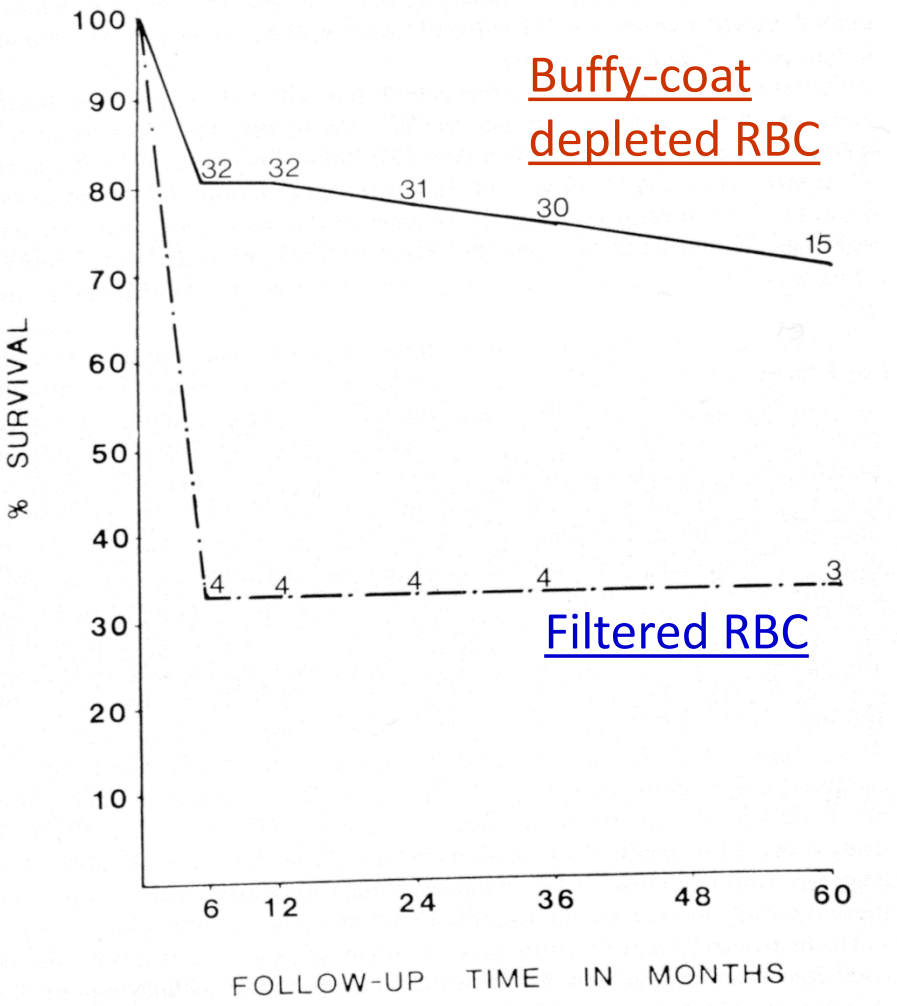


Figure 5.2. Kidney graft survival in the prospective blood transfusion study. The ——— line represents the patients who have received 1 *leukocyte-poor* blood transfusion prospectively. The —.—. line is the group of patients who received 1 or 3 *leukocyte-free* blood transfusions prior to transplantation. The overall difference is significant ($p = 0.007$).

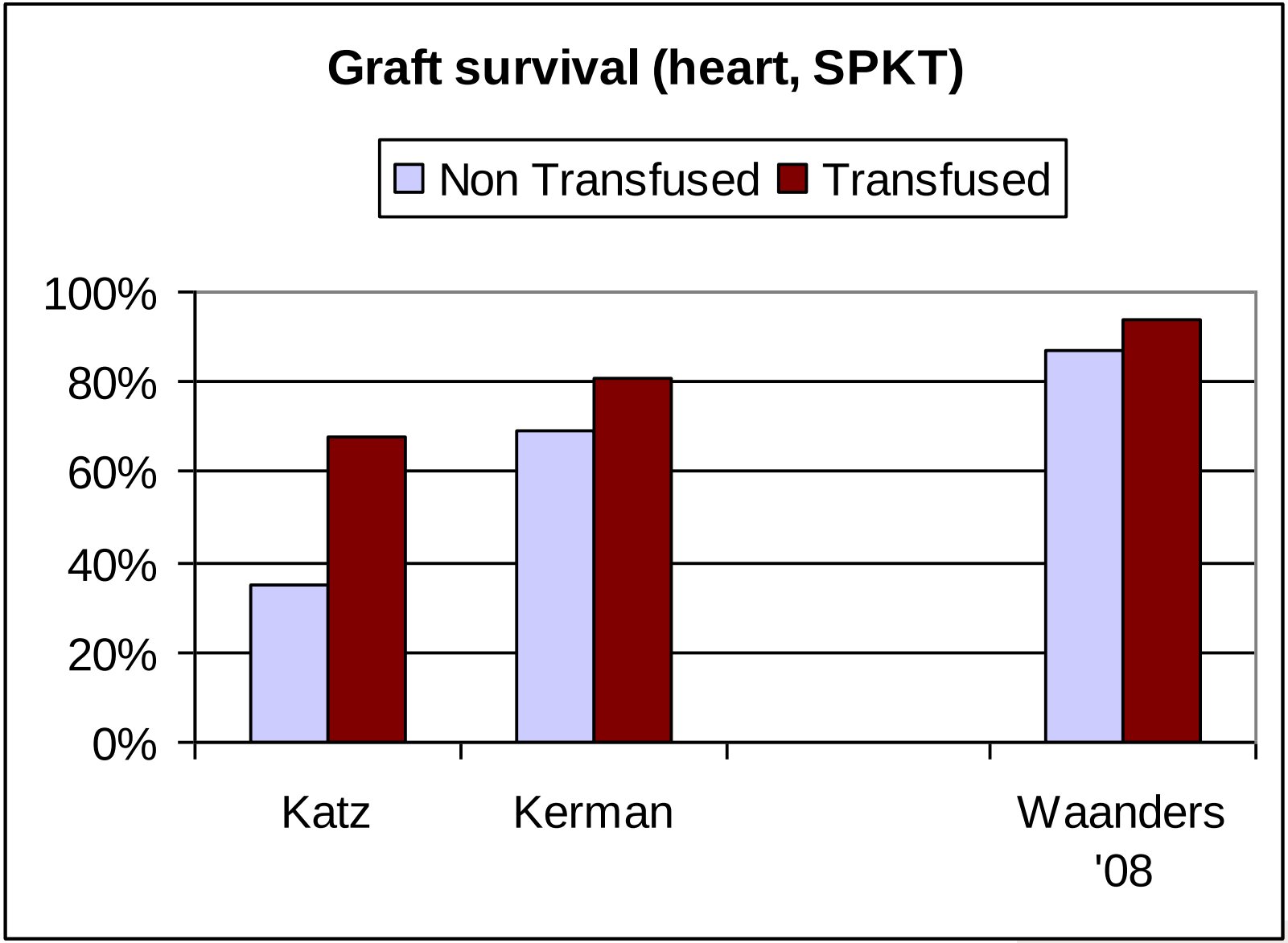
G.G. Persijn, Thesis 1985

Kidney graft survival:
Transfusies met gefiltreerd (WBC-arm) bloed geeft GEEN extra graft survival.

"Transfusie effect"

a.k.a. "TRIM"
Transfusion Related ImmunoModulation

TRIM & orgaantransplantatie



Hoewel het gunstige effect bij transplantaties nog steeds aanwezig lijkt, ook met de moderne immunosuppressiva, worden pre-transplantatie transfusies vrijwel nergens meer toegepast.

Als belangrijkste redenen hiervoor noemt men het risico op TTI en alloimmunisatie.

TRIM

TRIM EFFECTS:

BENEFICIAL

1. Enhanced survival of renal allografts
2. Reduced recurrence rate of Crohn's disease

DELETERIOUS

1. Increased recurrence rate of resected malignancies
2. Increased incidence of postoperative bacterial infections
3. Activation of endogenous CMV or HIV infection
4. Increased short-term (up to 3-month) mortality

Studies

CRAB-studie (1987-1990)
cancer recurrence, infecties, alloimmmunisatie
LD vs PC bij colorectale carcinomen
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Cancer Recurrence And Blood transfusion

Recidief:
Wordt vaker gezien in patiënten die bloedtransfusies hebben ontvangen

Gesuggereerde mechanismes bij colorectale carcinomen:

- Micrometastases (BM), immunosurveillance inhibited
  (Munich, M. Heiss et al)

- Confounder, complexe (rectale) chirurgie
  (Rotterdam, O. Busch et al)

CRAB

		Non-transfused	Transfused	p
Total population	At risk (N)	**251**	**446**	
	Survival (%)	72.9	59.6	<0.001
	Recurrence (%)	24.3	29.8	0.13
	Loc. Rec. (%)			
	Reg. Rec. (%)			
	Dist. Rec. (%)			
Rectum/r-s patients	At risk (N)	**96**	**243**	
	Survival (%)	67.7	56.0	*0.06*
	Recurrence (%)	25.0	35.4	*0.09*
	Loc. Rec. (%)			
	Reg. Rec. (%)			
	Dist. Rec. (%)			

Van de Watering '01

Immunomodulatie door bloed transfusie: Systemisch of lokaal?

Complexe chirurgie: Systemisch of lokaal?

CRAB

		Non-transfused	Transfused	p
Total population	At risk (N)	**251**	**446**	
	Survival (%)	72.9	59.6	<0.001
	Recurrence (%)	24.3	29.8	0.13
	Loc. Rec. (%)	*7.6*	*11.9*	*0.09*
	Reg. Rec. (%)	*4.0*	*6.1*	*0.29*
	Dist. Rec. (%)	*18.7*	*18.4*	*0.92*
Rectum/r-s patients	At risk (N)	**96**	**243**	
	Survival (%)	67.7	56.0	*0.06*
	Recurrence (%)	25.0	35.4	*0.09*
	Loc. Rec. (%)	*9.4*	*15.6*	*0.18*
	Reg. Rec. (%)	*2.1*	*6.6*	*0.16*
	Dist. Rec. (%)	*19.8*	*20.6*	*0.99*

Van de Watering '01

Zowel de transfusies als het recidief lijken veroorzaakt door de meer complexe (rectum) surgery

CRAB

		Non-transfused	Transfused	p
Total population	At risk (N)	**251**	**446**	
	Survival (%)	72.9	59.6	<0.001
	Recurrence (%)	24.3	29.8	0.13

Er is een verschil in recidieven tussen wel/niet getransfundeerde patienten ...

		Total	PCwbc	Filtered	p
Total population	At risk (N)	697	360	337	
	Survival (%)	64.4	63.6	65.3	0.69
	Recurrence (%)	27.8	27.8	27.9	0.99

Er is géén verschil in recidieven tussen de verschillende bloedproducten
Terwijl PCwbc wel verbeterde graft survival gaf en gefiltreerde RBC niet.

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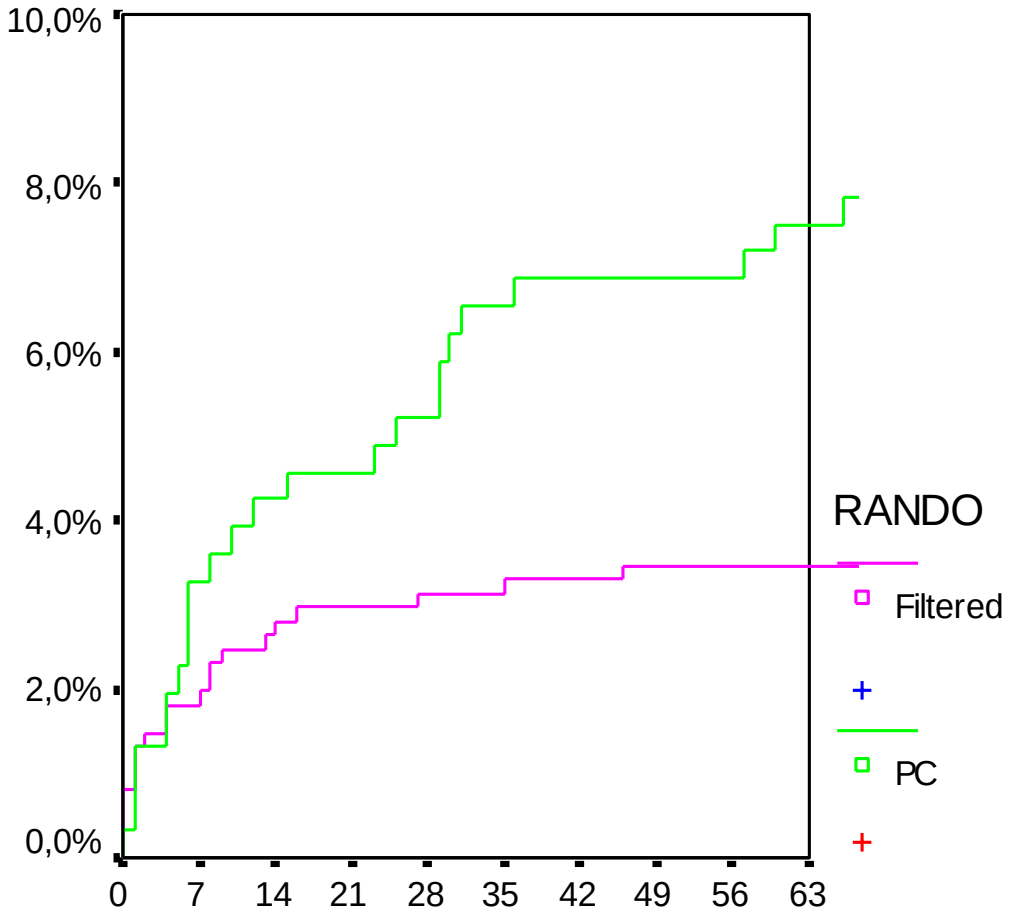
LAL

	PC		FF		SF	
	N	%	N	%	N	%
All patients	306	7.8	305	3.6	303	3.3
Transfusion status						
0 BT	12	0	20	5.0	16	0
Transfused	294	8.2	285	3.5	287	3.5
Number of transfusions						
1-3 BT's	125	1.6	117	0.9	113	1.8
4-6 BT's	98	5.1	99	1.0	104	1.9
7-10 BT's	39	10.3	39	2.6	43	4.7
> 10 BT's	32	40.6	30	23.3	27	14.8

Van de Watering '98

Mortality



Days postsurgery

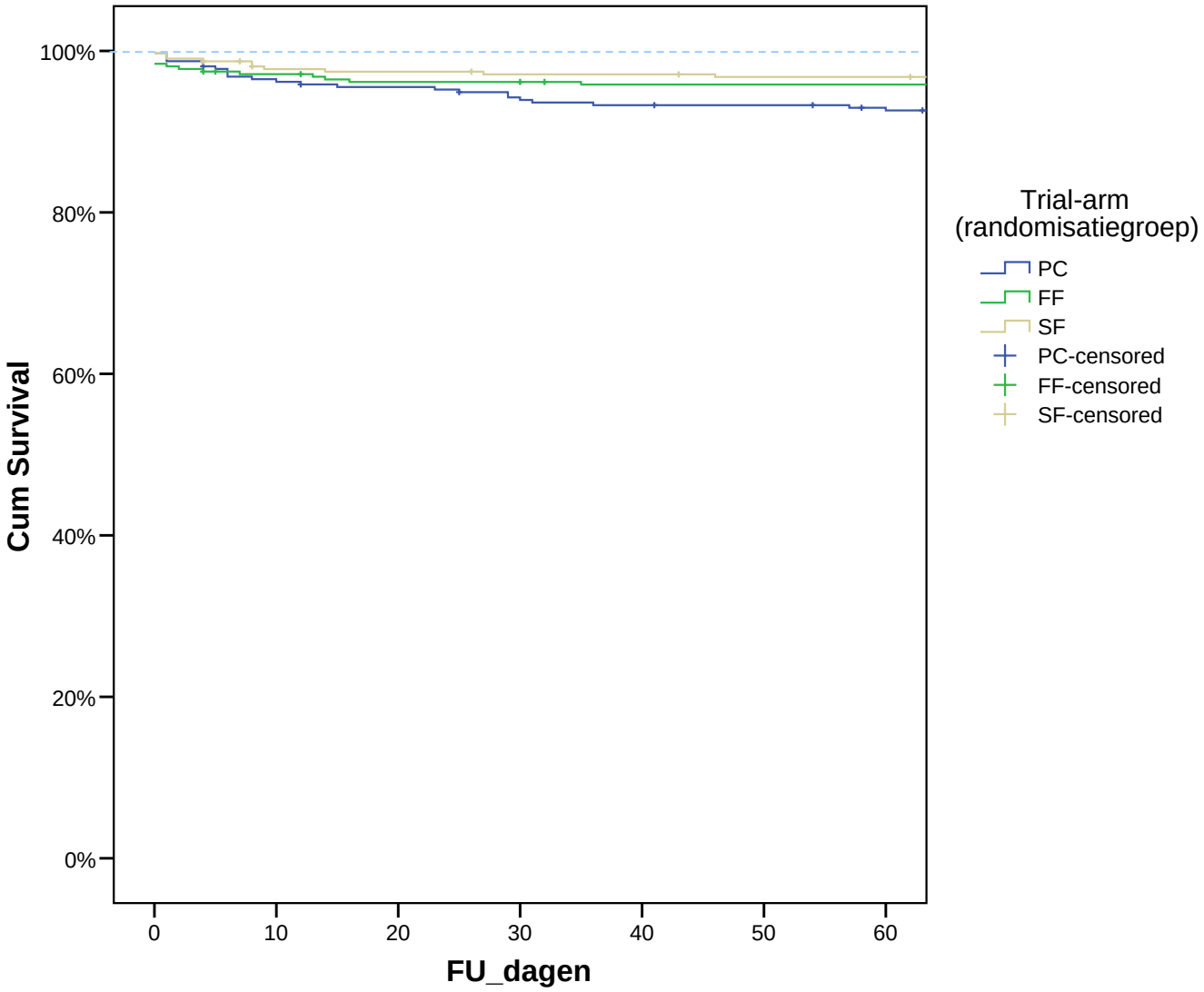
Van de Watering '98

Cardiac mortality
(arrhythmia, MI)
PC = LR

Additional mortality in non-filtered group: MODS

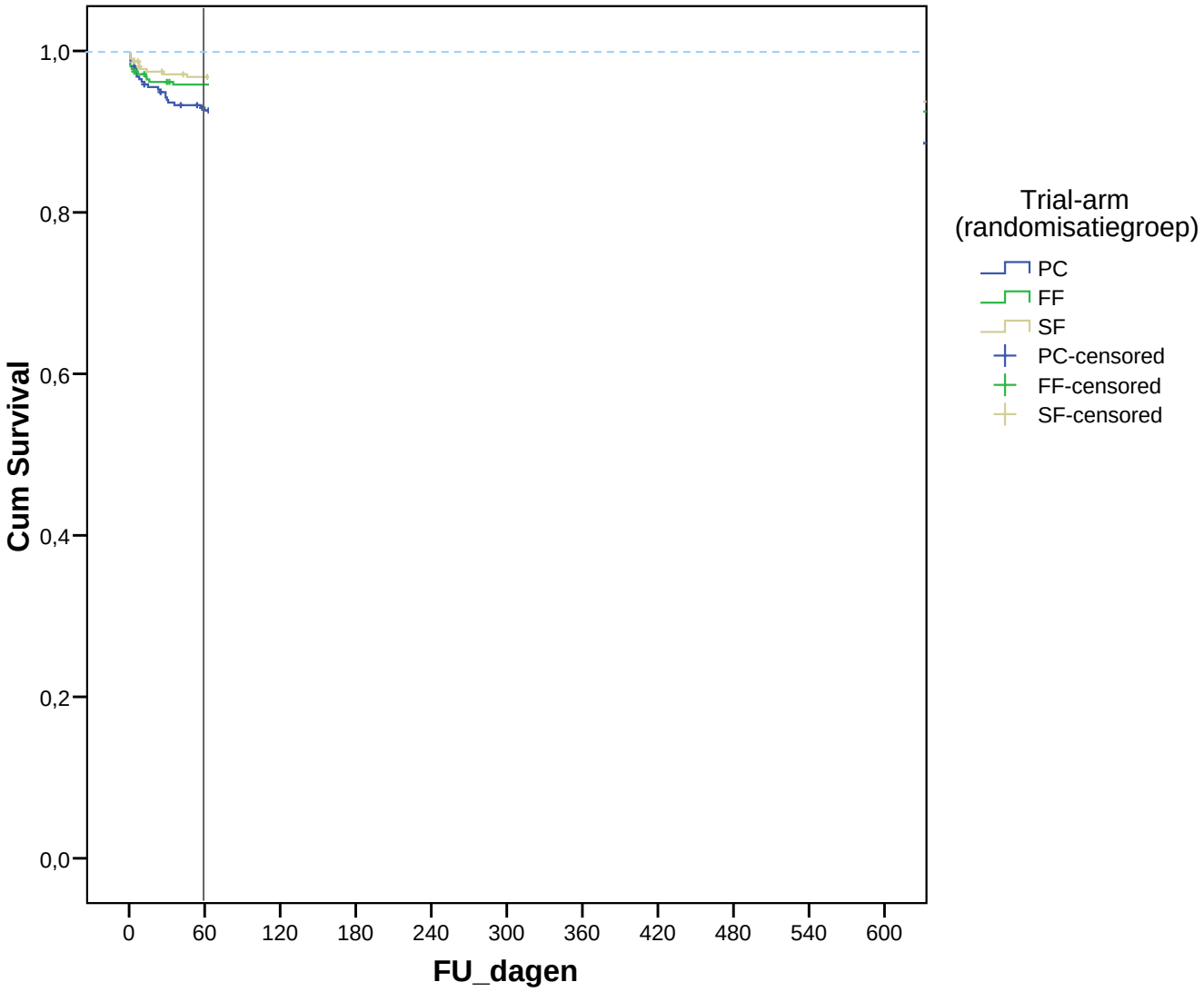
LAL

short term (60d)



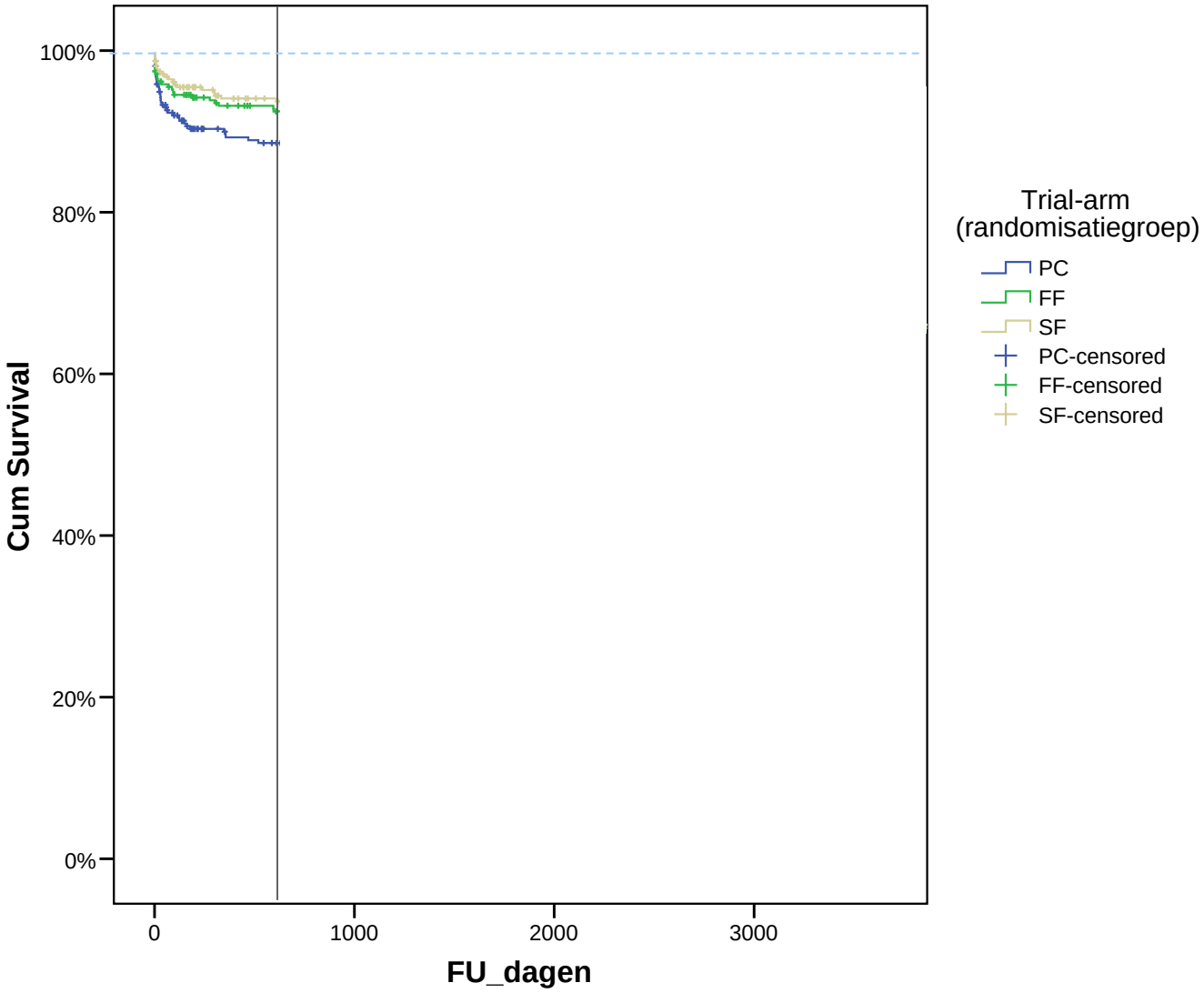
LAL

medium term (600d)



LAL

long-term (10y)



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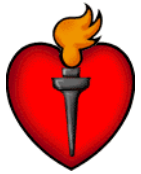
TacTicS-GE

- 19 Ziekenhuizen
- Patienten: Acuut AAA
  Electief AAA
  GE-onco
- Randomisatie: PC vs LD (=FF)
- Stratificatie (Zh; Type chirurgie)
- Power: 18% vs 10% mortaliteit

  $\alpha = 0.05$; $\beta = 0.1$

  => 625 pat./trialarm

TacTicS-Th



- Twee centra (AMC; LUMC)
- Type chirurgie: Klep ± CABG
- Randomisatie: PC vs LD (=FF)
- Stratificatie (Zh; Type chirurgie)
- Power: 15% vs 5% mortaliteit

  $\alpha = 0.05$; $\beta = 0.1$

  => 207 pat./trialarm

ISBT 2004, Edinburgh: Leucodepletion: Is There a Step Too Far?

~~Evidence based medicine~~

Believers & non-believers

"… we recommend universal adoption (of LR) even if we are not certain of its benefits." Carson & Berlin, Can J Anesth 2004

"Although opponents of ULR are correct in their assertion that the clinical value of ULR has not been unequivocally demonstrated, I believe that the application of this rigid standard … is not appropriate and will retard advances in transfusion medicine" Sweeney, Am J Clin Pathol 2001

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RBC bewaarduur

Max.age
RBC > 21d

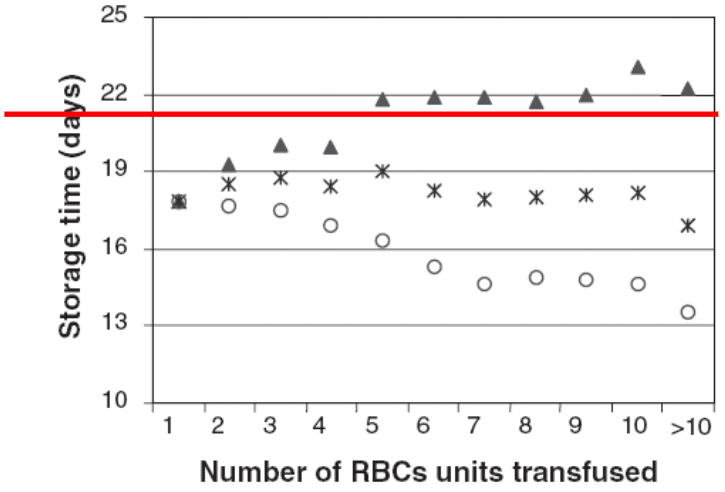

Fig. 2. Correlation of the total number of transfusions with the storage times of RBCs. (▲) Mean maximum storage time; (✳) mean average storage time; (○) mean minimum storage time.

TABLE 3. Association of RBC storage time with length of ICU stay and 30-day mortality

Characteristic	Crude model		Adjusted model	
	Hazard ratio (95% CI)	p Value	Hazard ratio (95% CI)	p Value
ICU stay ("risk" of ICU discharge)				
Storage time*				
Mean of all RBC units (weeks)	1.01 (0.96-1.06)	0.64	1.01 (0.96-1.06)	0.76
Oldest RBC unit (weeks)	0.95 (0.91-0.99)	0.015	1.01 (0.96-1.05)	0.80
Youngest RBC unit (weeks)	1.05 (1.01-1.10)	0.029	1.00 (0.96-1.05)	0.90
All RBCs > 18 days†	0.97 (0.89-1.06)	0.52	0.98 (0.89-1.09)	0.74
30-day survival				
Storage time*				
Mean of all RBC units (weeks)	1.13 (0.89-1.43)	0.34	0.96 (0.72-1.29)	0.80
Oldest RBC unit (weeks)	0.85 (0.69-1.05)	0.13	0.98 (0.76-1.25)	0.85
Youngest RBC unit (weeks)	1.33 (1.04-1.68)	0.021	0.93 (0.71-1.23)	0.62
All RBCs > 18 days†	0.97 (0.58-1.61)	0.89	0.76 (0.42-1.37)	0.35

* Storage time is analyzed as a continuous variable, expressed in weeks.

† In the analysis "All RBCs > 18 days," the 950 patients receiving all RBCs older than 18 days are compared to the 945 patients receiving all RBCs younger than 18 days. The 837 patients receiving RBCs both younger and older than 18 days or RBCs stored for 18 days were excluded from this analysis.

RBC bewaarduur

apples

oranges

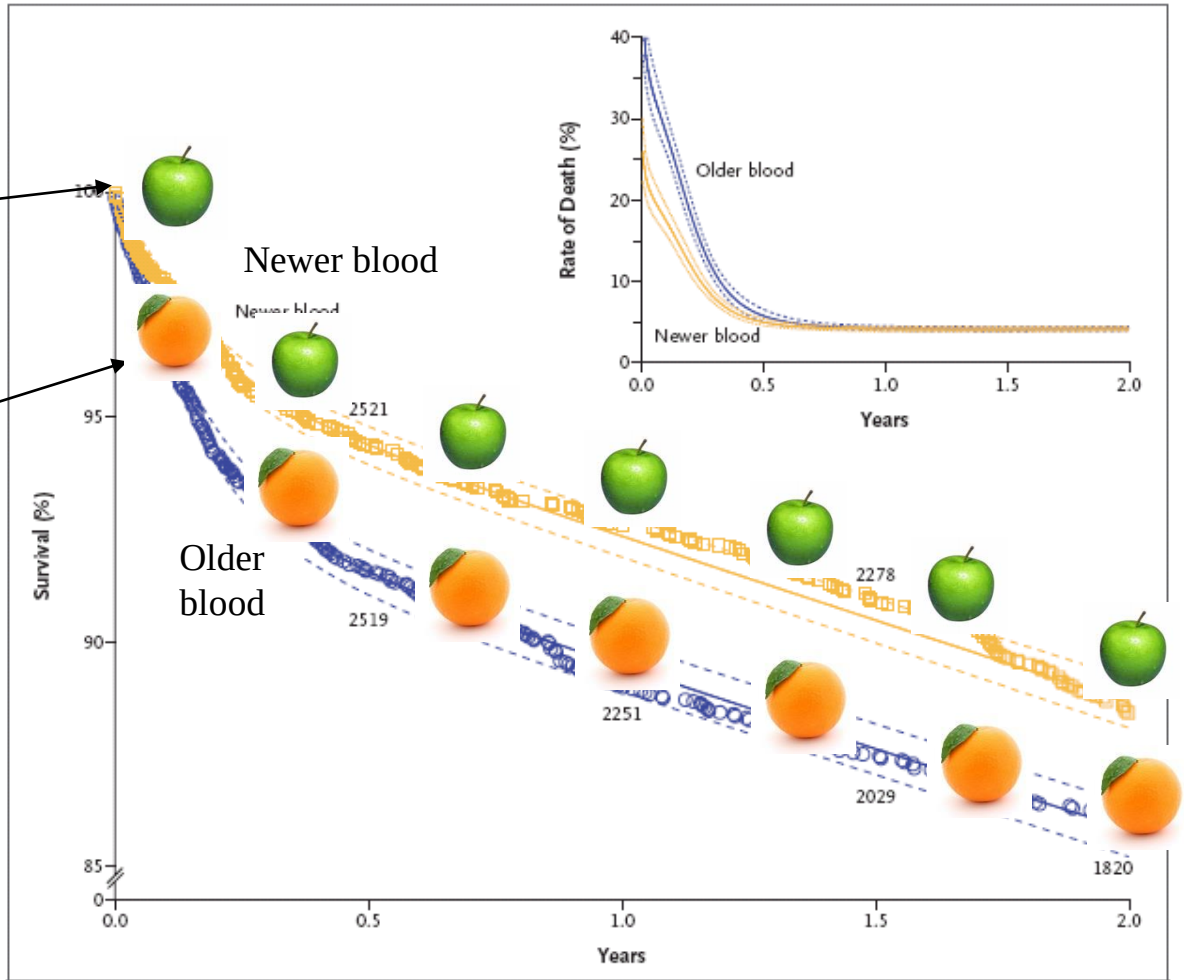

Figure 3. Kaplan–Meier Estimates of Survival and Death.

The curves show data from 2872 patients who were given exclusively newer blood (stored for 14 days or less) and

In this un-adjusted comparison,

determined by the Kaplan–Meier method, is superimposed on the parametric survival function estimator. In this un-adjusted comparison, the percentage of patients receiving older blood who survived was lower than the percentage of those receiving newer blood who survived, especially during the initial follow-up period.

RBC bewaarduur

NCT00326924 "ARIPI" (Canada, D. Fergusson)

<7d vs St.; Composite endpoint in premature infants

ISRCTN44878718 "**ABLE"** (Canada, J. Lacroix)

<8d vs St.; 90 day mortality in high risk ICU patients

NCT00991341 (01274390) Recess (RECAP) (US, NHLBI)

<11d vs >20d; MODS (O_2 saturation) compl.cardiac surgery

ISRCTN08188744 "INFORM" (CAN,US R. Barty)

Freshest vs St.; In-hosp.mort. in all transfused patients >18y

NCT01638416 "TRANSFUSE" (ANZIC, B.Ady)

Freshest vs St.; 90-d.mortality in ICU patients >18y

RBC bewaarduur

RBC bewaarduur

IPDMA

Marie Steiner MD
Taye Hamza

Richard J Cook
Jamie Cooper
Dean Fergusson
Craig French
Paul Hebert
Nancy Heddle
Jacques Lacroix
Zoe McQuilten
Simon Stanworth
Steve Sloan
Darrell Triulzi
Marialena Trivella
Leo van de Watering

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IPDMA: ??