The 2018 Frankfurt consensus conference on patient blood management: towards better evidence

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DRK-Blutspendedienst
Baden-Württemberg - Hessen

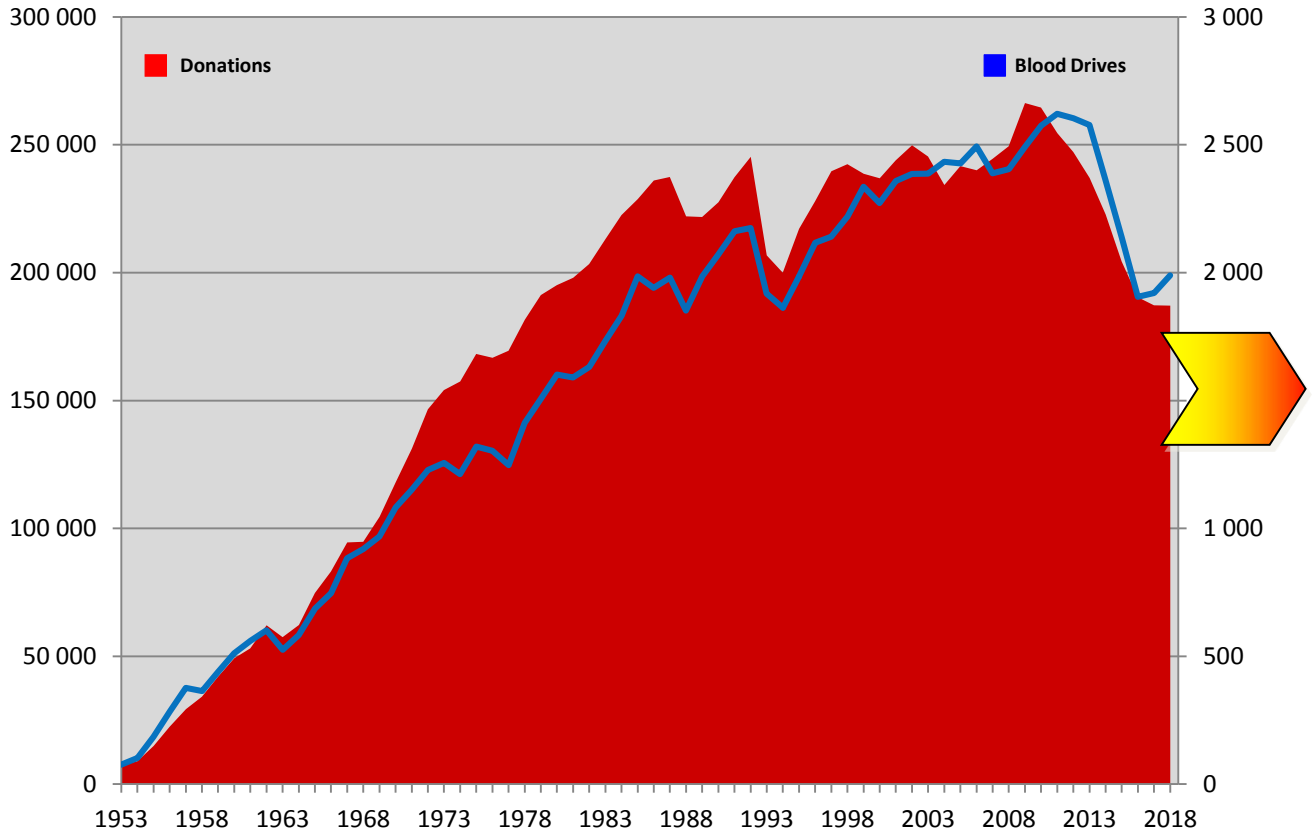
SPENDE BLUT

BEIM ROTEN KREUZ

für dich

Blood Products: Demand in Hessen

Development of blood donations in Hessen 1953 - 2018

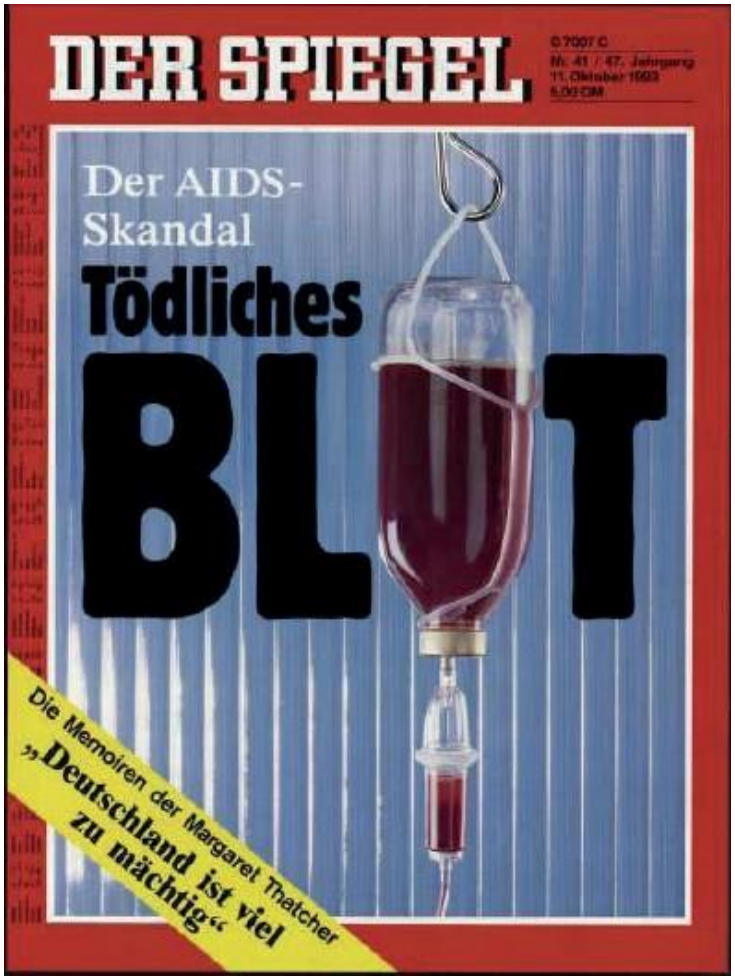


- surgery
- intensive care
- traumatology
- emergency care
- hematology
- oncology
- transplant. medicine
- pediatrics
- gynecology
- Urology
- .....

Adverse Events of Blood Transfusion – Real Ones and Supposed Ones

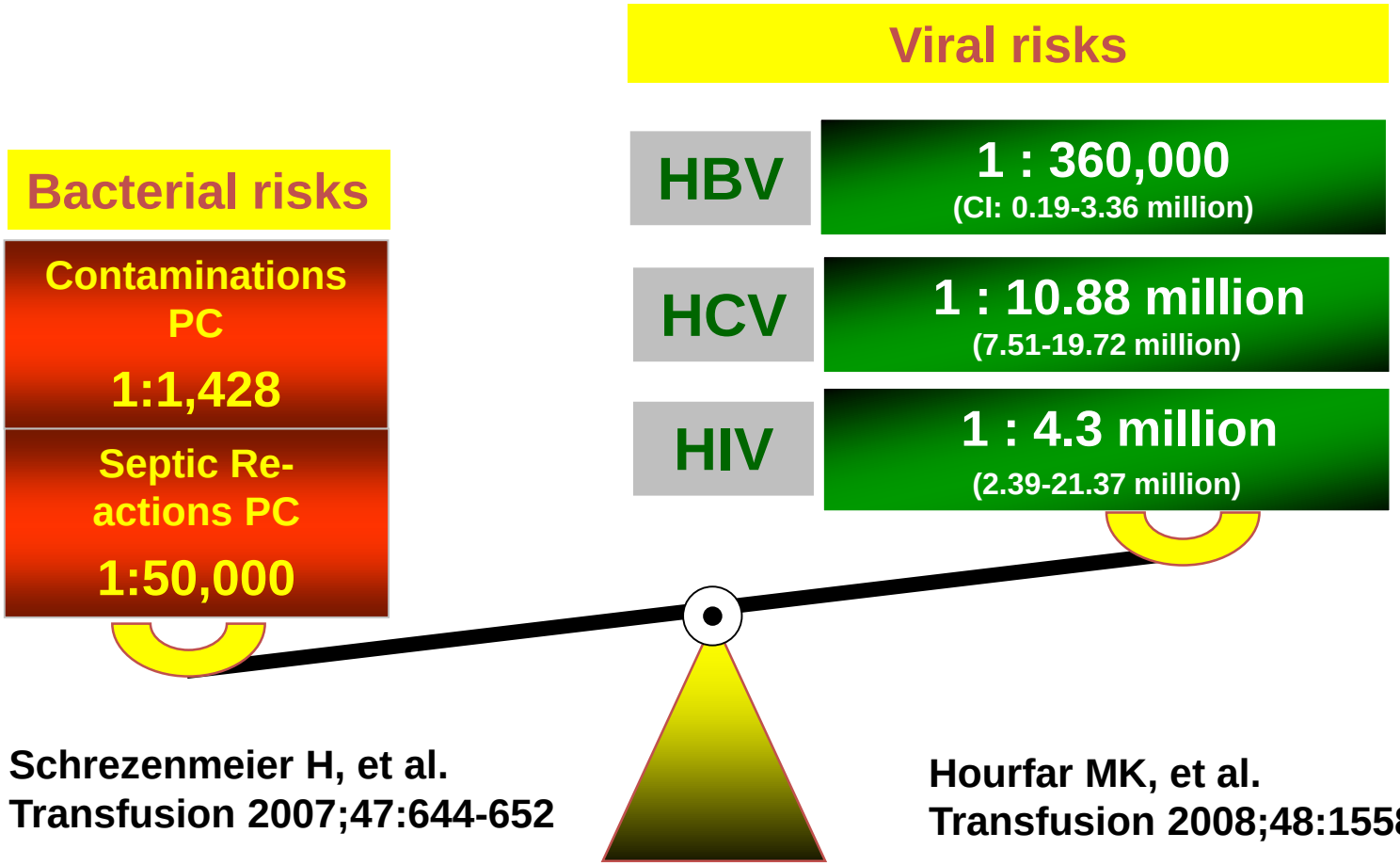
- Transfusion associated viral infections
- Transfusion associated bacterial infections
- TRIM: Transfusion induced immunomodulation in the recipient
  - increased infection rate
  - impaired wound healing
  - higher risk of tumor spread (metastases)
- Risk of mix-up/wrong blood in tube (WBIT)
- Higher morbidity
- Higher mortality
- Increase in hospital stay
- Higher costs
- etc.

Blood/HIV/AIDS Scandal



- June 1982: First case of HIV transmission via blood product in Germany
- In sum, 1,846 out of 3,927 (47%) hemophilia patients in Germany were infected by HIV-1
- Triggered by this disaster, activities to increase blood safety were intensified.

Calculated residual risk for TTI (2007)



Schrezenmeier H, et al.
Transfusion 2007;47:644-652

Hourfar MK, et al.
Transfusion 2008;48:1558-1566

Gutes Blut - Schlechtes Blut

Bitteres Umdenken in der Transfusionsmedizin

(Stand: November 2014)

Die Janusköpfigkeit der Bluttransfusion

28. November 2014 Herz-Kreislauf-System, Immunsystem, Infek

Todesgefahr Bluttransfusionen

Eine Bluttransfusion kann Leukämie auslösen!

Böses Blut - Kehrtwende in der Intensivmedizin

Transfusionen

Das gefährliche Blut

Bewerten Ärzte das Risiko von Transfusionen für den Empfänger falsch? Eine Gruppe von Medizinern setzt sich für ein Umdenken ein.

16.01.2015, von LUCIA SCHMIDT

Technology Review
DAS MAGAZIN FÜR INNOVATION

Weniger hilft mehr

Kaum ein Mediziner zweifelt am Sinn von Blutkonserven. Dabei zeigen immer mehr Studien, dass sie oft mehr schaden als nützen.

Transfusionen sind riskant

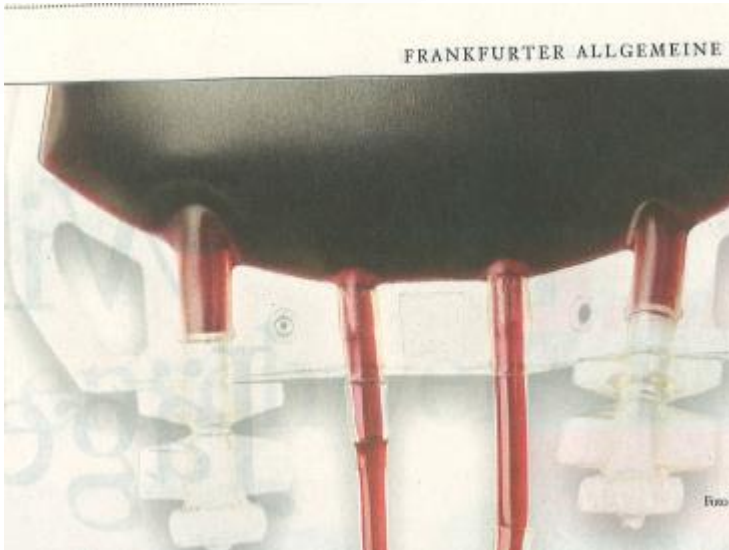
von Stefanie Liedtke

Süddeutsche.de Wissen

17. Mai 2010, 20:51 Gefahr durch Transfusion

Tödliche Blutspende

"In Österreich wird zu schnell Blut verabreicht"



„Evil Blood“ and „Red Danger“ … ?

Patient Blood Management

Rotes Gold

Die Zahl der Operationen hierzulande steigt kontinuierlich und damit auch der Bedarf an Blutkonserven. Ihr Vorrat wird künftig aufgrund medizinischer und gesellschaftlicher Veränderungen aber schrumpfen. Immer mehr Kliniken setzen deshalb bei der Suche nach Alternativen zur Bluttransfusion auf individuelles Patient Blood Management. Ein entsprechendes Programm zur Stärkung patienteneigener Blutressourcen und Vermeidung unnötiger Fremdbluttransfusionen wurde im April mit dem Preis für Patientensicherheit 2016 ausgezeichnet.

Prof. Dr. Patrick Meybohm, Dr. Suma Choorapoikayil, Prof. Dr. Dr. Kai Zacharowski

In Deutschland werden jedes Jahr rund 15 Millionen Patienten operiert. Musallam et al. berichten in einer Gesamtkohorte von 227 425 stationären Patienten von einer Prävalenz der präoperativen Anämie von 30 Prozent (1). Häufig wird die Blutarmut vor oder während der OP durch die Gabe von Erytrozytenkonzentraten (EK) temporär behoben, ohne aber einer potentiellen Diagnose mit gezielter Therapie nachzugehen. Entscheidend ist hierbei, dass sowohl eine präoperative Anämie an sich als auch die EK-Transfusion mit einem

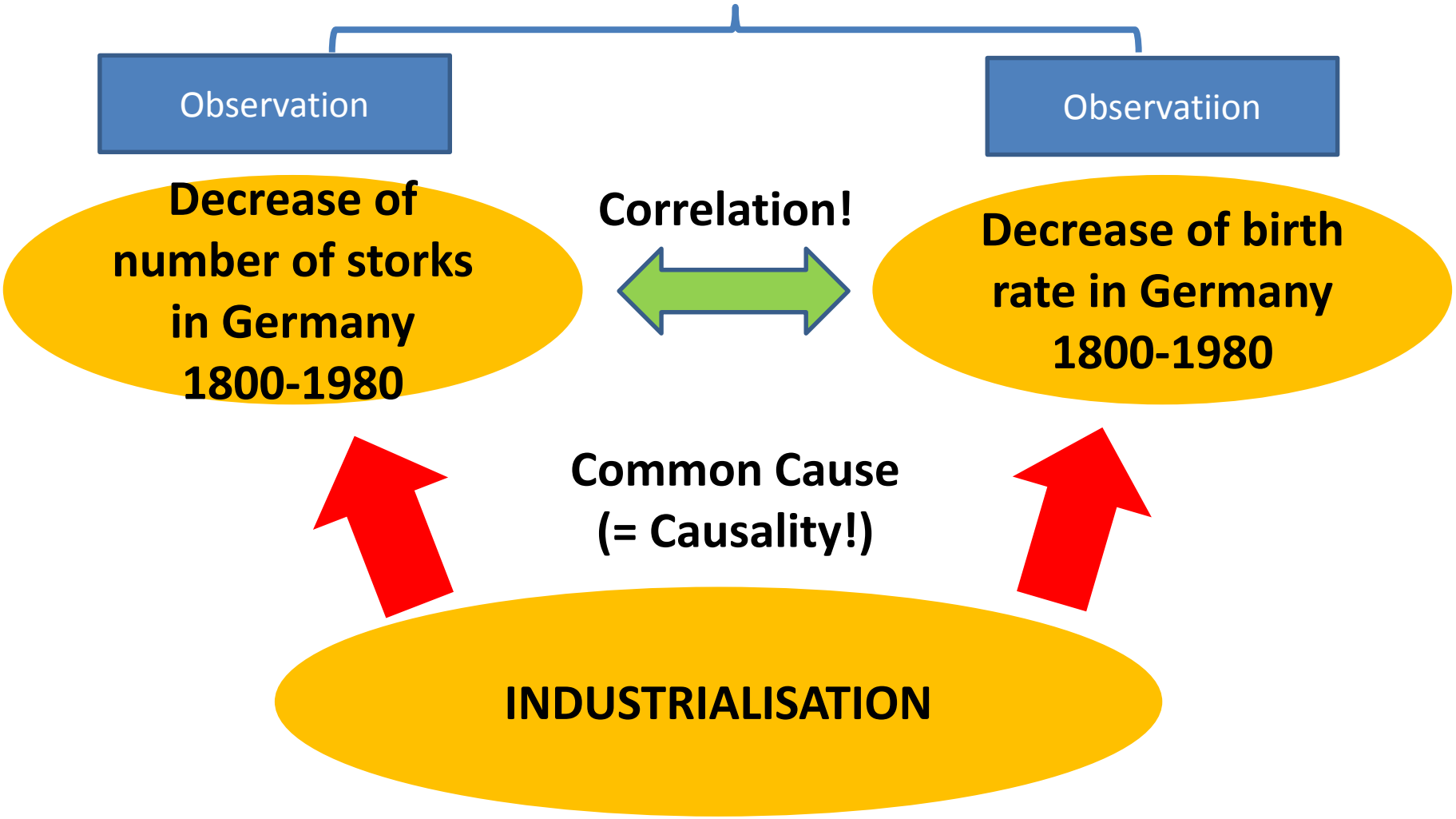
men der OP und der Nachversorgung assoziiert sind. Insgesamt weist die gängige Praxis der EK-Transfusion weltweit eine sehr hohe Variabilität auf. Deutschland liegt mit mehr als 50 transfundierten EK pro 1000 Einwohner an der Spitze in Europa und weltweit – im Vergleich: Australien 36, Niederlande 34, Norwegen 42, Großbritannien 36, Schweiz 41 (2, 3). Blutkonserven werden künftig aber aufgrund medizinischer

und gesellschaftlicher Veränderungen zu einer zunehmend knappen Ressource. Ein vielversprechender Lösungsansatz ist das multidisziplinäre Patient Blood Management-(PBM-)Konzept, dessen Umsetzung die Weltgesundheitsorganisation (WHO) seit 2010 fordert (4). Im Zentrum des PBM stehen drei Säulen.

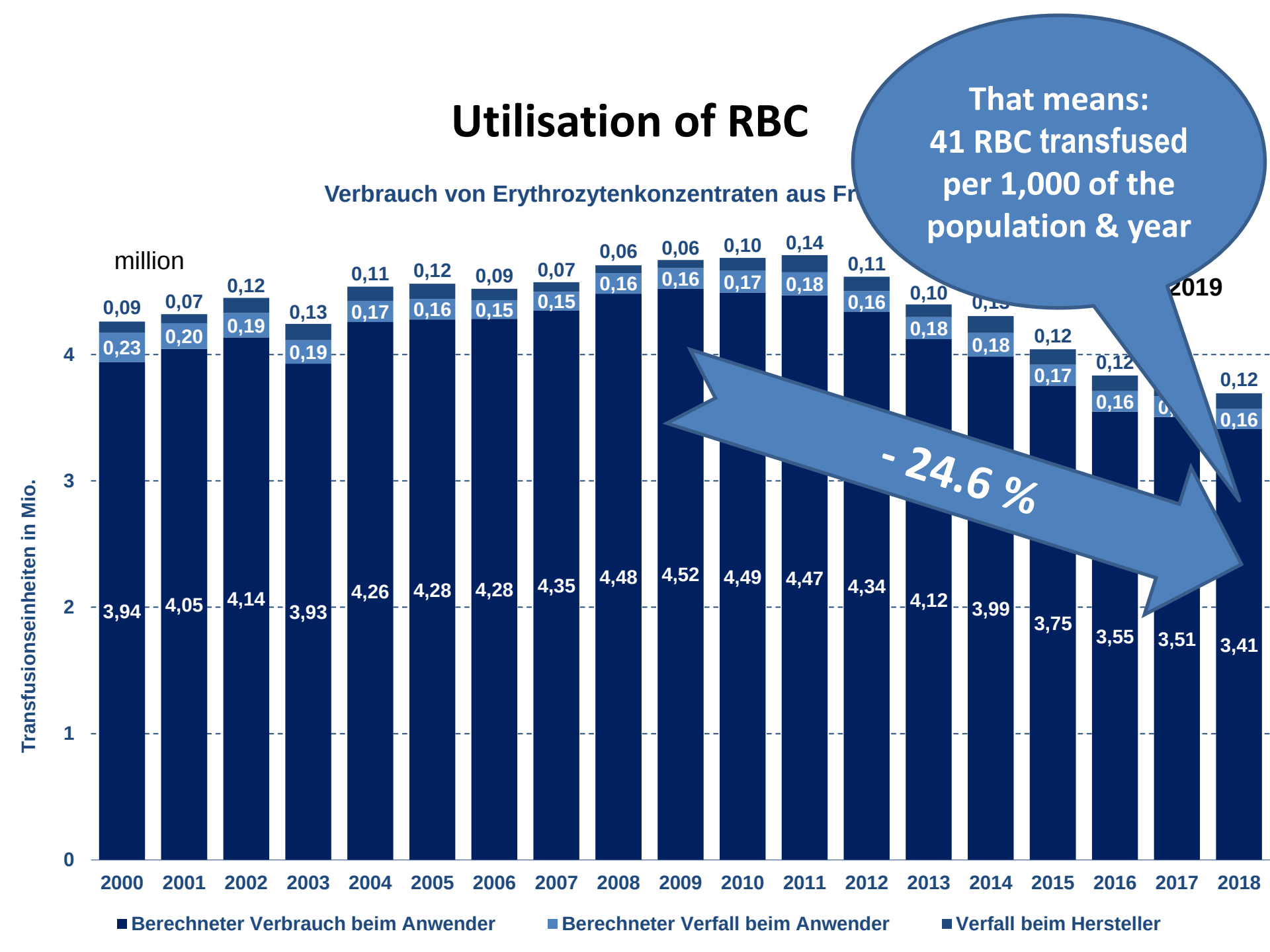
nahdran
MAGAZIN DES B. BRAUN KONZERNS FÜR FACHKREISE
2/16

“Die Zeit“ Title April 27, 2017

Correlation ≠ Causality

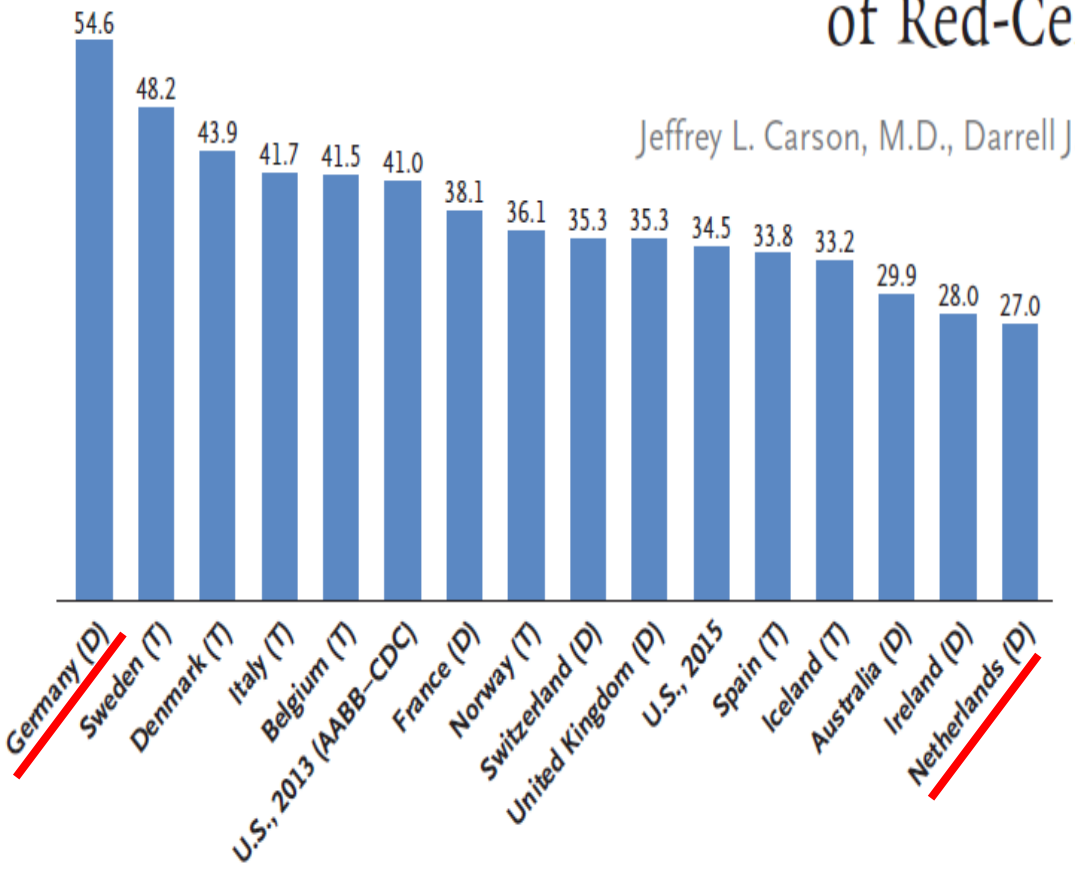


Utilisation of RBC



Indications for and Adverse Effects of Red-Cell Transfusion

Jeffrey L. Carson, M.D., Darrell J. Triulzi, M.D., and Paul M. Ness, M.D.

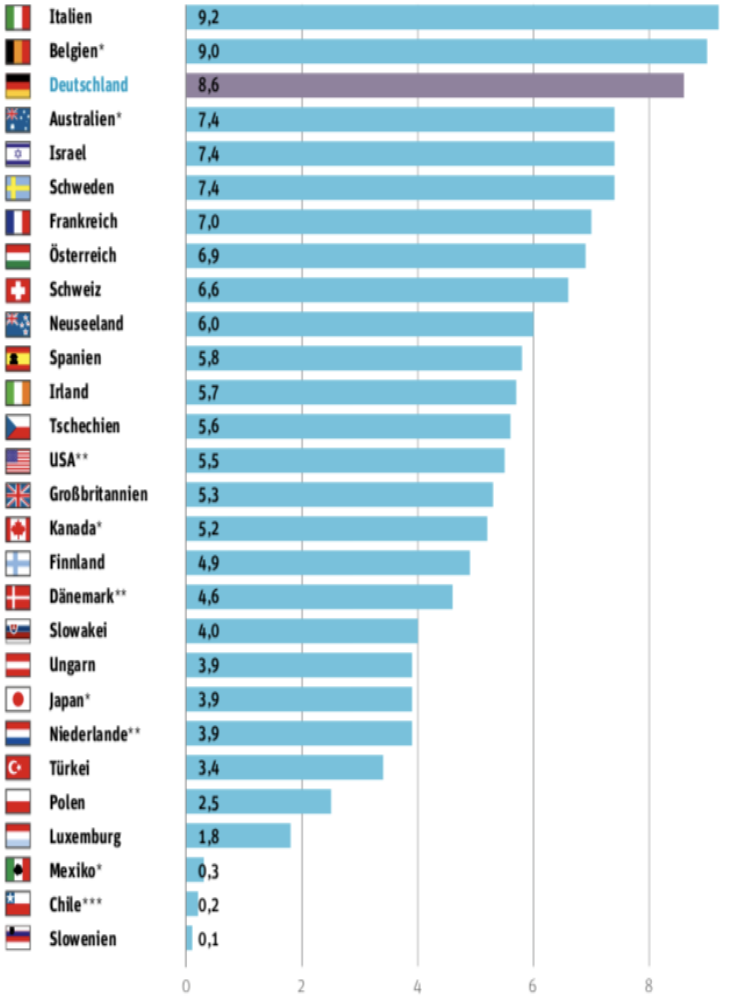


N Engl J Med 2017;377:1261-72.
DOI: 10.1056/NEJMra1612789

Figure 3. Transfusion Rates in the United States in 2013 and 2015, as Compared with Rates in Other Developed Countries.

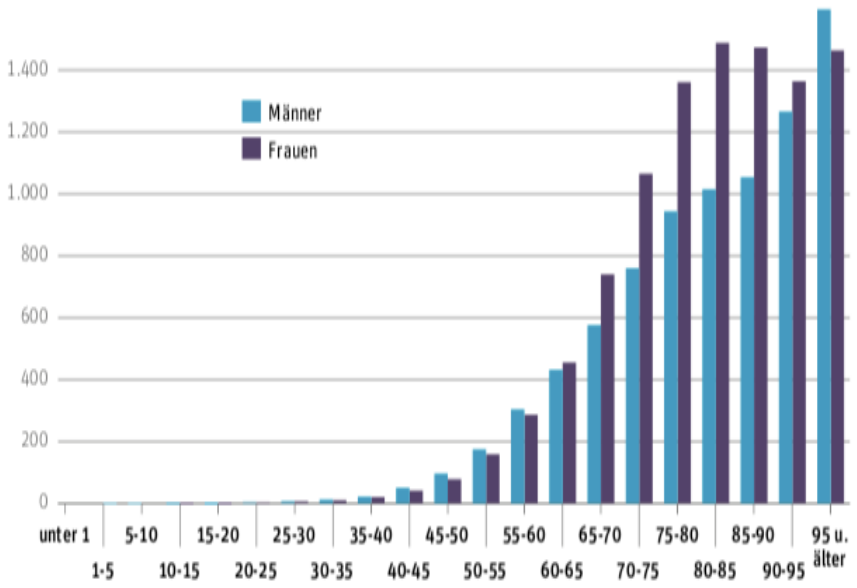
The number above each bar is the number of transfused red-cell units per 1000 population. Transfusion rates in the United States in 2013 and 2015 are compared with the most recent data on transfusion rates in Europe (2013).[33] The U.S. rate of transfusion in 2013, 41.0 units per 1000 population, is the midpoint of the rates estimated separately on the basis of the 2013 AABB Blood Collection, Utilization, and Patient Blood Management Survey[28] (40.3 units per 1000) and the 2013 Centers for Disease Control and Prevention (CDC) NBCUS (41.7 units per 1000).[29] The U.S. rate of transfusion in 2015, 34.5 units per 1000, is based on the 2015 NBCUS.[30] The data shown are for distributed (D) or transfused (T) units of blood, which are typically nearly equivalent.

Hematopoietic Stem Cell Transplantation (left)
Cases per 100,000 inhabitants (2012)
Right: Total hip replacement (THR) in Germany 2012
Numbers per 100, 000 inhabitants per age group and sex



Quelle: OECD Gesundheitsstatistik 2014.
Anmerkung: * = OECD-Daten aus dem Jahr 2011, ** = OECD-Daten aus dem Jahr 2010, *** = OECD-Daten aus dem Jahr 2009.

Abbildung 6:
Anzahl der Hüftgelenkersatz-Operationen je 100.000 Einwohner in Deutschland nach Altersgruppen und Geschlecht im Jahr 2012



Quelle: DRG-Statistik 2012; Statistiken zu den Versichertenzahlen in PKV und GKV; eigene Berechnung.
Anmerkung: Die Zahlen beziehen sich ausschließlich auf Erstimplantate und Prothesenwechsel. Prothesenentfernungen sind nicht enthalten.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 29, 2011 VOL. 365 NO. 26

Liberal or Restrictive Transfusion in High-Risk Patients after Hip Surgery

Jeffrey L. Carson, M.D., Michael L. Terrin, M.D., M.P.H., Helaine Noveck, M.P.H., David W. Sanders, M.D., Bernard R. Chaitman, M.D., George G. Rhoads, M.D., M.P.H., George Nemo, Ph.D., Karen Dragert, R.N., Lauren Beaupre, P.T., Ph.D., Kevin Hildebrand, M.D., William Macaulay, M.D., Courtland Lewis, M.D., Donald Richard Cook, B.M.Sc., M.D., Gwendolyn Dobbin, C.C.R.P., Khwaja J. Zakriya, M.D., Fred S. Apple, Ph.D., Rebecca A. Horney, B.A., and Jay Magaziner, Ph.D., M.S.Hyg., for the FOCUS Investigators*

FOCUS

FOCUS The NEW ENGLAND JOURNAL of MEDICINE

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Liberal or Restrictive Transfusion in High-Risk Patients after Hip Surgery

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CONCLUSIONS

A liberal transfusion strategy, as compared with a restrictive strategy, did not reduce rates of death or inability to walk independently on 60-day follow-up or reduce in-hospital morbidity in elderly patients at high cardiovascular risk. (Funded by the National Heart, Lung, and Blood Institute; FOCUS ClinicalTrials.gov number, NCT00071032.)

N Engl J Med 2011;365:2453-62.

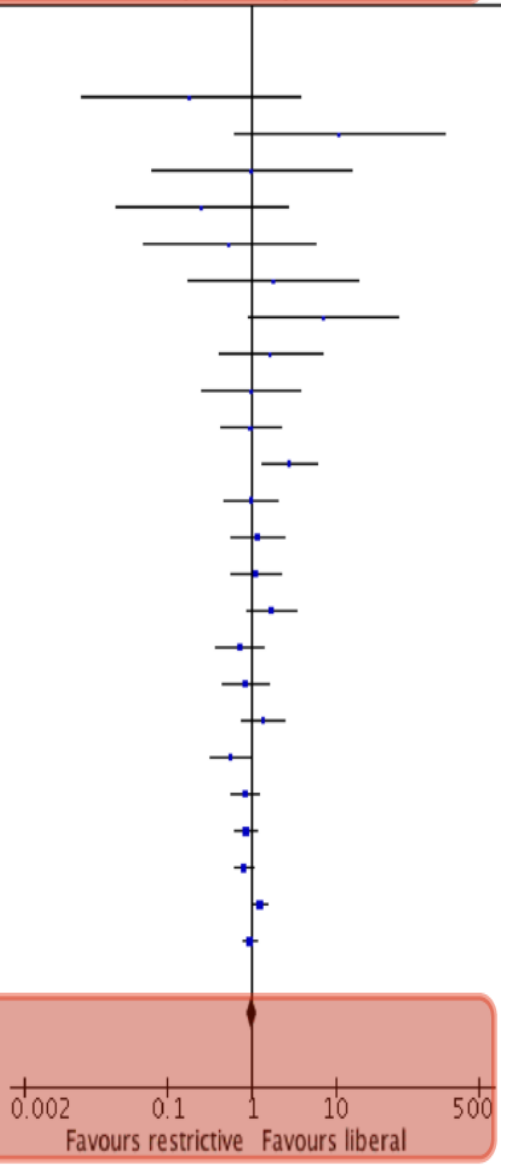
30-Day Mortality

Carson JL et al American Heart Journal 2018

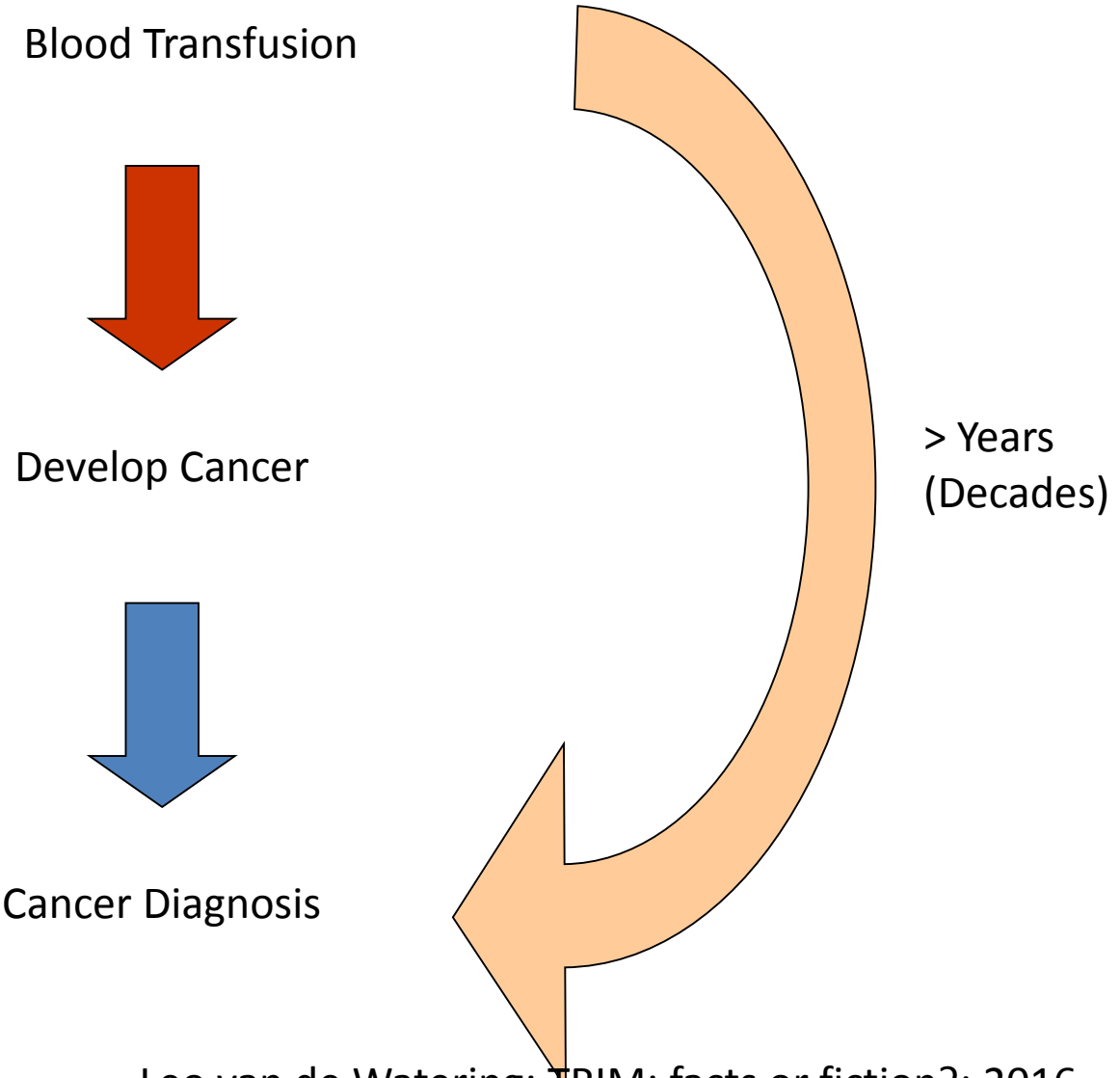
Study or Subgroup	Restrictive Events	Restrictive Total	Liberal Events	Liberal Total	Weight	Risk Ratio M-H, Random, 95% CI
Laine 2017	0	40	0	40		Not estimable
Lotke 1999	0	62	0	65		Not estimable
Blair 1986	0	26	2	24	0.2%	0.19 [0.01, 3.67]
Foss 2009	5	60	0	60	0.3%	11.00 [0.62, 194.63]
Carson 1998	1	42	1	42	0.3%	1.00 [0.06, 15.47]
DeZern 2016	1	59	2	30	0.4%	0.25 [0.02, 2.69]
Webert 2008	1	29	2	31	0.4%	0.53 [0.05, 5.58]
Cooper 2011	2	23	1	21	0.4%	1.83 [0.18, 18.70]
Carson 2013	7	55	1	55	0.5%	7.00 [0.89, 55.01]
Parker 2013	5	100	3	100	1.1%	1.67 [0.41, 6.79]
Bush 1997	4	50	4	49	1.2%	0.98 [0.26, 3.70]
Hébert 1995	8	33	9	36	2.7%	0.97 [0.42, 2.22]
de Almeida 2015	23	101	8	97	3.2%	2.76 [1.30, 5.87]
Lacroix 2007	14	320	14	317	3.4%	0.99 [0.48, 2.04]
Hajjar 2010	15	249	13	253	3.4%	1.17 [0.57, 2.41]
Palmieri 2017	16	168	15	177	3.8%	1.12 [0.57, 2.20]
Gregersen 2015	21	144	12	140	3.9%	1.70 [0.87, 3.32]
Walsh 2013	12	51	16	49	4.2%	0.72 [0.38, 1.36]
Jairath 2015	14	257	25	382	4.2%	0.83 [0.44, 1.57]
Murphy 2015	26	1000	19	1003	4.7%	1.37 [0.76, 2.46]
Villanueva 2013	19	416	34	417	5.3%	0.56 [0.32, 0.97]
Carson 2011	43	1009	52	1007	7.9%	0.83 [0.56, 1.22]
Mazer 2017	74	2427	87	2429	10.2%	0.85 [0.63, 1.15]
Hébert 1999	78	418	98	420	11.4%	0.80 [0.61, 1.04]
Bergamin 2017	84	151	67	149	12.6%	1.24 [0.99, 1.55]
Holst 2014	168	502	175	496	14.4%	0.95 [0.80, 1.13]
Total (95% CI)		**7792**		**7889**	**100.0%**	**1.00 [0.86, 1.16]**
Total events	641		660			

Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 34.44$, df = 23 (P = 0.06); $I^2 = 33\%$

Test for overall effect: Z = 0.02 (P = 0.99)



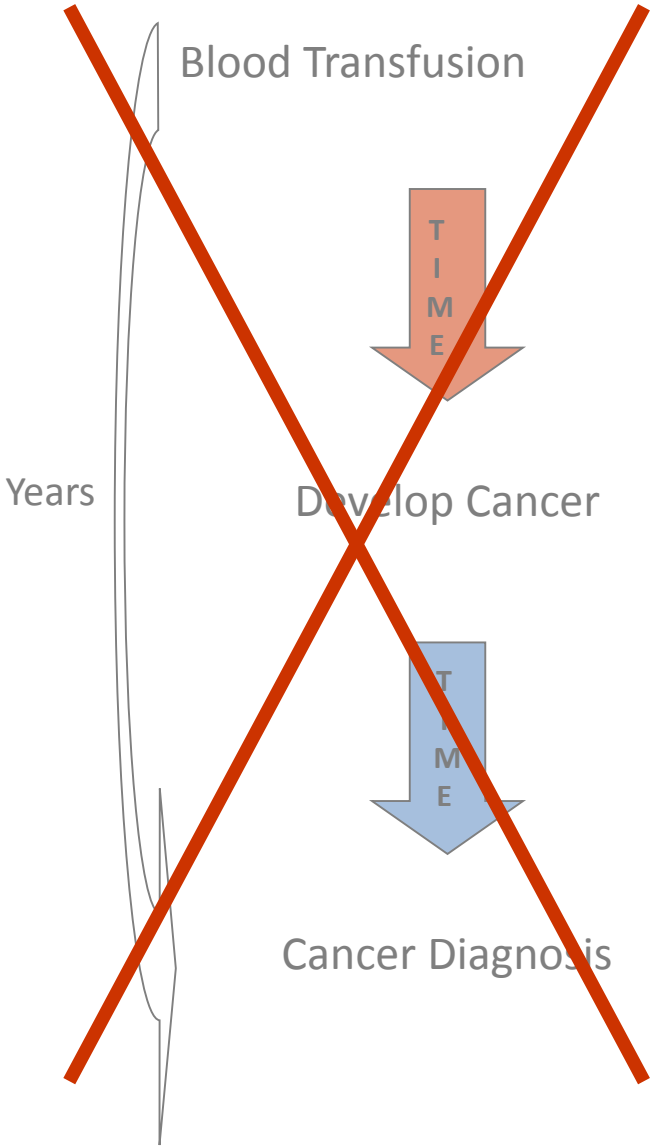
TRIM & new malignancies

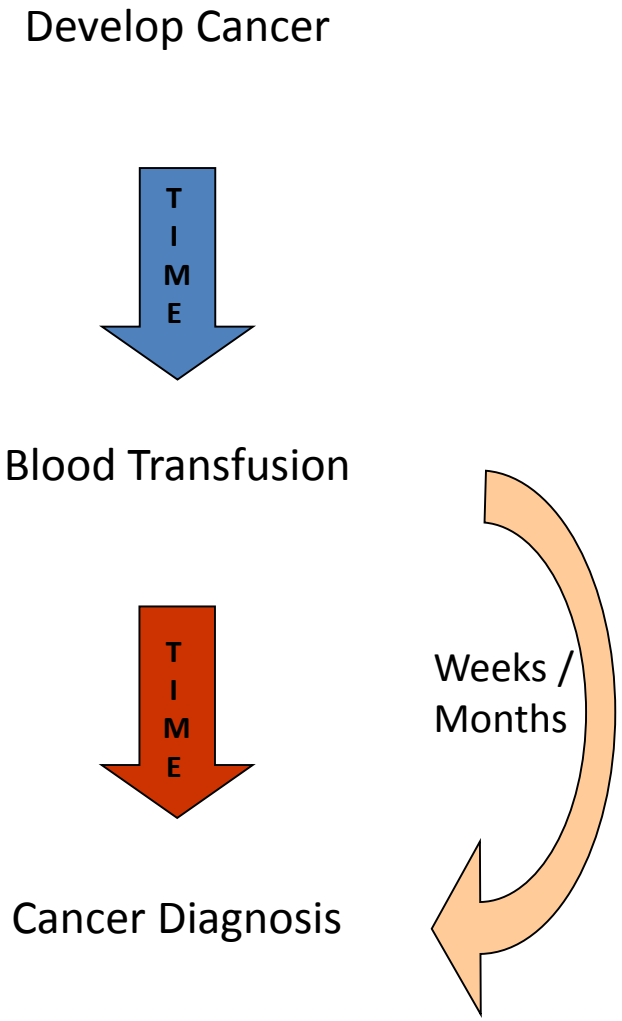


Leo van de Watering: TRIM: facts or fiction?; 2016

TRIM

Reverse causality





Leo van de Watering: TRIM: facts or fiction?; 2016

TRIM

Leo van de Watering: TRIM: facts or fiction?; 2016

The weakening association over time is clearly shown in plots

Meta-analysis completely ignored time-interval information

"Our analysis shows … increased risk of developing NHL in those patients who received allogeneic RBC transfusions."

Castillo '10

Liberal versus restrictive blood transfusion strategy: 3-year survival and cause of death results from the FOCUS randomised controlled trial

FOCUS

Jeffrey L Carson, Frederick Sieber, Donald Richard Cook, Donald R Hoover, Helaine Noveck, Bernard R Chaitman, Lee Fleisher, Lauren Beaupre, William Macaulay, George G Rhoads, Barbara Paris, Aleksandra Zagorin, David W Sanders, Khwaja J Zakriya, Jay Magaziner

Source: Lancet 2015;385:1183-9

Summary

Background Blood transfusion might affect long-term mortality by changing immune function and thus potentially increasing the risk of subsequent infections and cancer recurrence. Compared with a restrictive transfusion strategy, a more liberal strategy could reduce cardiac complications by lowering myocardial damage, thereby reducing future deaths from cardiovascular disease. We aimed to establish the effect of a liberal transfusion strategy on long-term survival compared with a restrictive transfusion strategy.

Findings Between July 19, 2004, and Feb 28, 2009, 2016 patients were enrolled and randomly assigned to the two treatment groups: 1007 to the liberal transfusion strategy and 1009 to the restrictive transfusion strategy. The median duration of follow-up was 3·1 years (IQR 2·4–4·1 years), during which 841 (42%) patients died. Long-term mortality did not differ significantly between the liberal transfusion strategy (432 deaths) and the restrictive transfusion strategy (409 deaths) (hazard ratio 1·09 [95% CI 0·95–1·25]; p=0·21).

Interpretation Liberal blood transfusion did not affect mortality compared with a restrictive transfusion strategy in a high-risk group of elderly patients with underlying cardiovascular disease or risk factors. The underlying causes of death did not differ between the trial groups. These findings do not support hypotheses that blood transfusion leads to long-term immunosuppression that is severe enough to affect long-term mortality rate by more than 20–25% or cause of death.

RBC & Cancer recurrence
Non-immunologic?

Prevention and Epidemiology

Cancer Research

High Serum Iron Is Associated with Increased Cancer Risk

Chi Pang Wen[1,2], June Han Lee[1], Ya-Ping Tai[1], Christopher Wen[3], Shiuan Be Wu[1], Min Kuang Tsai[1], Dennis P.H. Hsieh[1,4], Hung-Che Chiang[5], Chao Agnes Hsiung[1], Chung Y. Hsu[6], and Xifeng Wu[7]

Iron and cancer: more ore to be mined

Suzy V. Torti[1] and Frank M. Torti[2]

Abstract | Iron is an essential nutrient that facilitates cell proliferation and growth. However, iron also has the capacity to engage in redox cycling and free radical formation. Therefore, iron can contribute to both tumour initiation and tumour growth; recent work has also shown that iron has a role in the tumour microenvironment and in metastasis. Pathways of iron acquisition, efflux, storage and regulation are all perturbed in cancer, suggesting that reprogramming of iron metabolism is a central aspect of tumour cell survival. Signalling through hypoxia-inducible factor (HIF) and WNT pathways may contribute to altered iron metabolism in cancer. Targeting iron metabolic pathways may provide new tools for cancer prognosis and therapy.

Leo van de Watering: TRIM: facts or fiction?; 2016

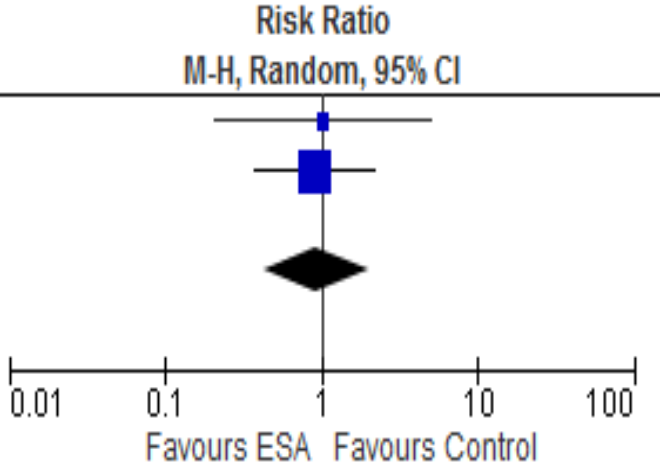
ESA versus No Treatment

CRITICAL OUTCOME: 45-day mortality

Study or Subgroup	ESA Events	ESA Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Weltert 2010	3	158	3	162	23.8%	1.03 [0.21, 5.00]
Weltert 2015	9	300	10	300	76.2%	0.90 [0.37, 2.18]
Total (95% CI)		**458**		**462**	**100.0%**	**0.93 [0.43, 2.01]**
Total events	12		13			

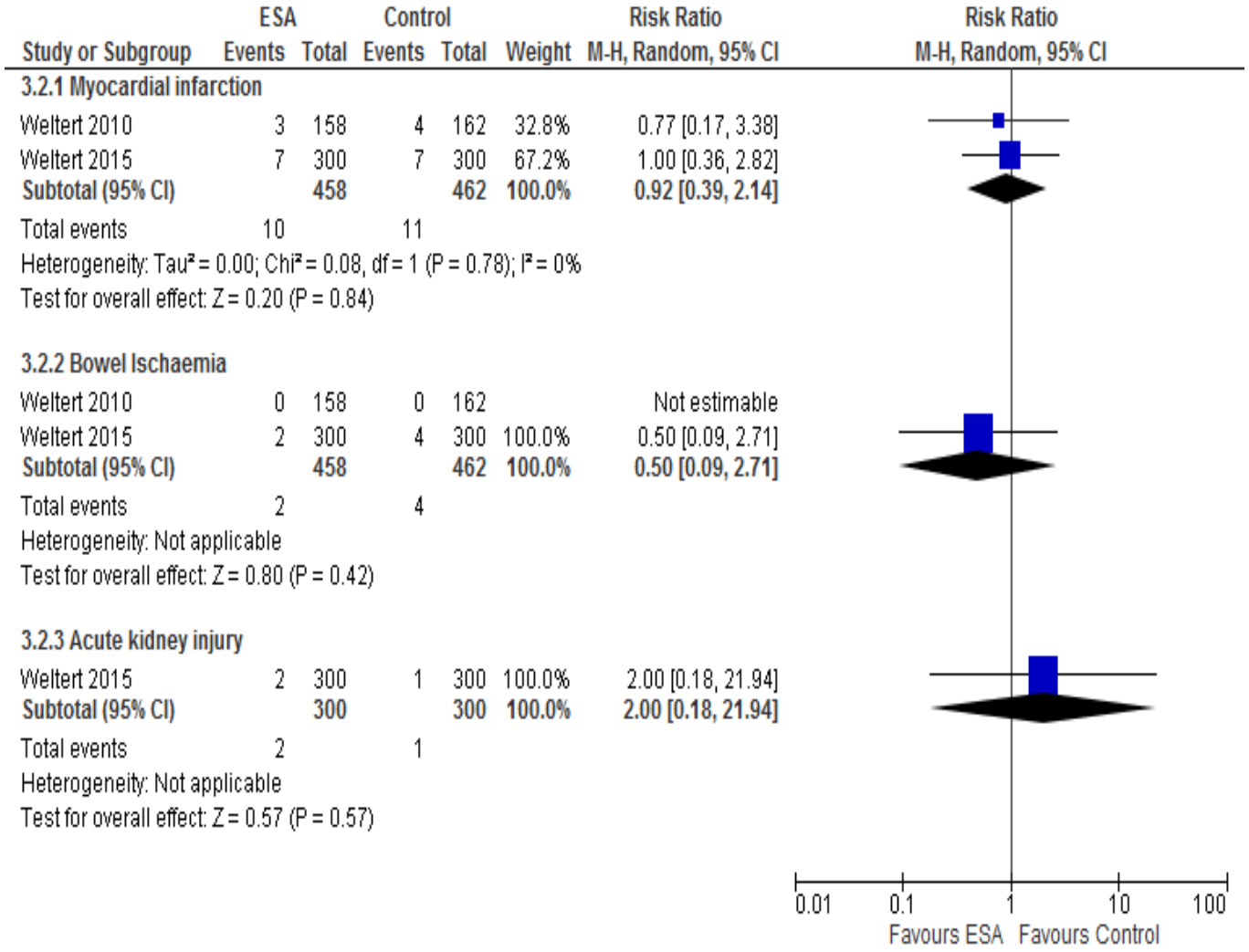
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.02$, df = 1 (P = 0.89); $I^2 = 0\%$

Test for overall effect: Z = 0.19 (P = 0.85)



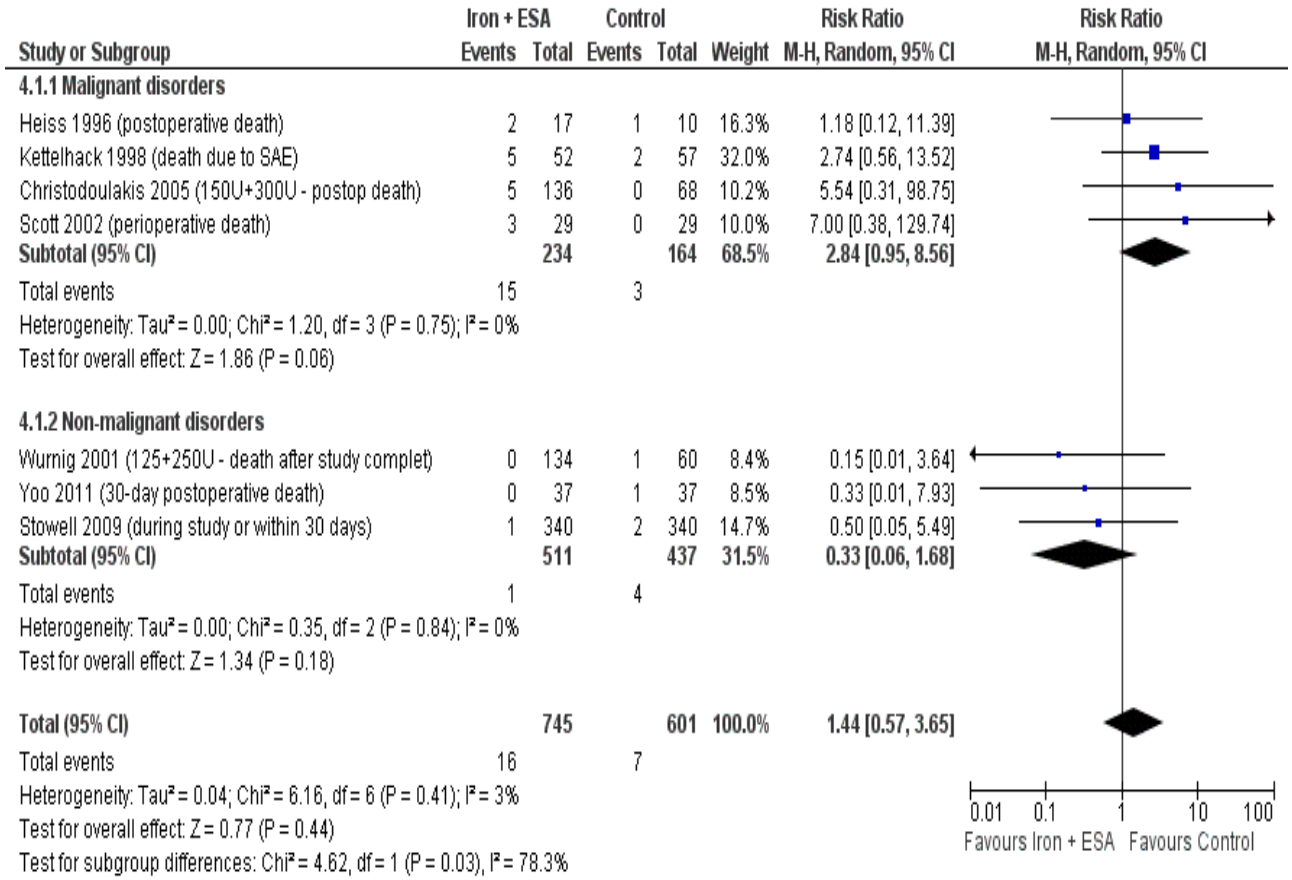
ESA versus No Treatment

CRITICAL OUTCOME: Anaemia-associated ischaemic events



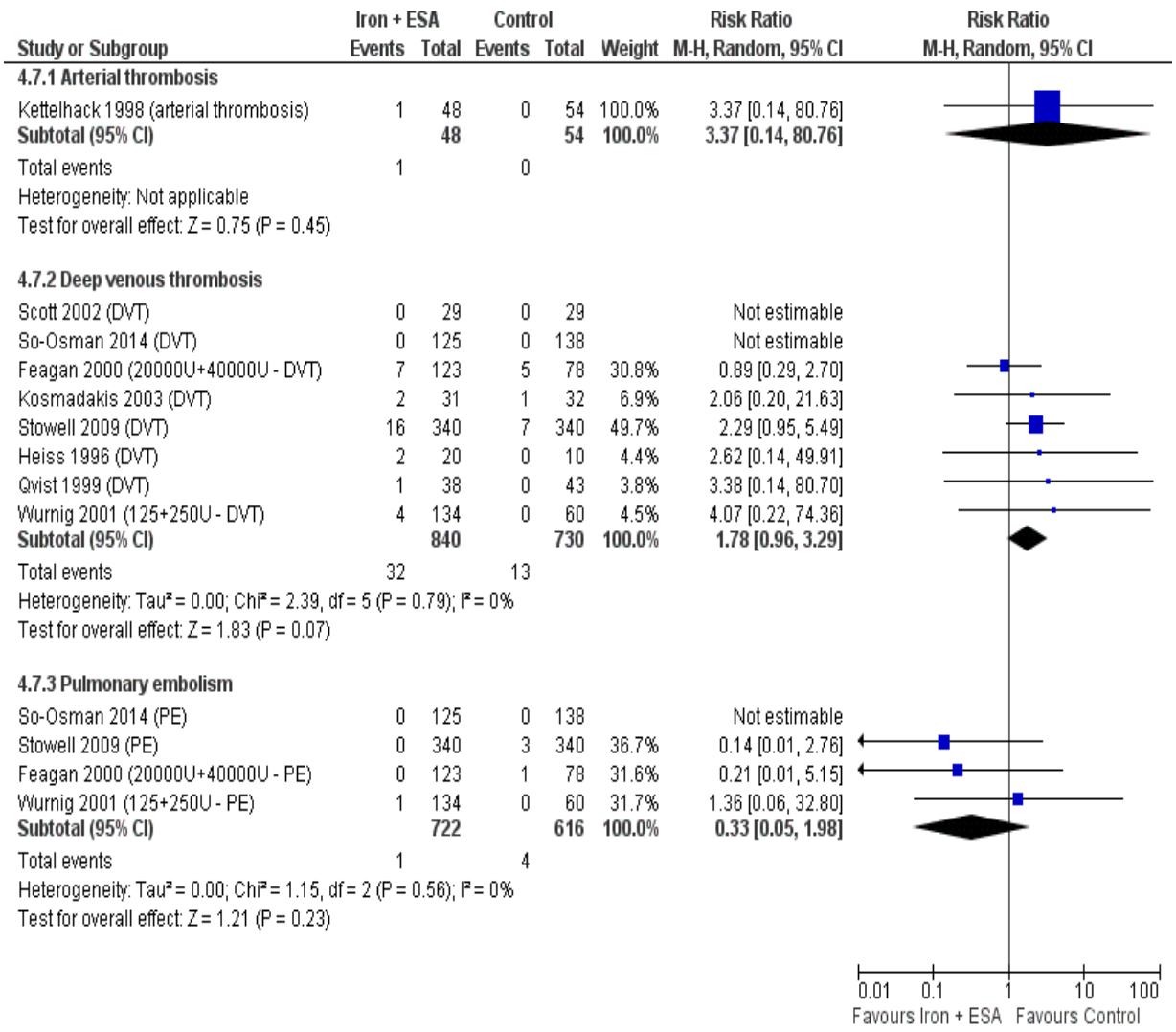
ESA + Iron versus Placebo/No Treatment

CRITICAL OUTCOME: Mortality



ESA + iron versus Placebo/No Treatment

CRITICAL OUTCOME: Thromboembolic events



International Consensus Conference towards Evidence-based Patient Blood Management
Frankfurt/Main, Germany, April 24 & 25, 2018

History of the ICC PBM Frankfurt 2018 Preparations

- Feb 2017: SciCom meeting, Frankfurt
- June 2017: Sponsors meeting, ISBT Copenhagen
- March 2017 – April 2018:

  12 SciCom teleconferences
- Jan/Feb 2018: 2 face-to-face meetings with SciSec and chairs, Frankfurt

- Dec 2017 – April 2018: 13 webinars
  - 2 SciCom webinars
  - 4 panellists webinars
  - 3 chairs webinars
  - 1 webinar rapporteurs
  - 1 tutorial rapporteurs
  - 2 speakers webinars

blood®
Prepublished online March 11, 2019;
doi:10.1182/blood-2018-10-877530

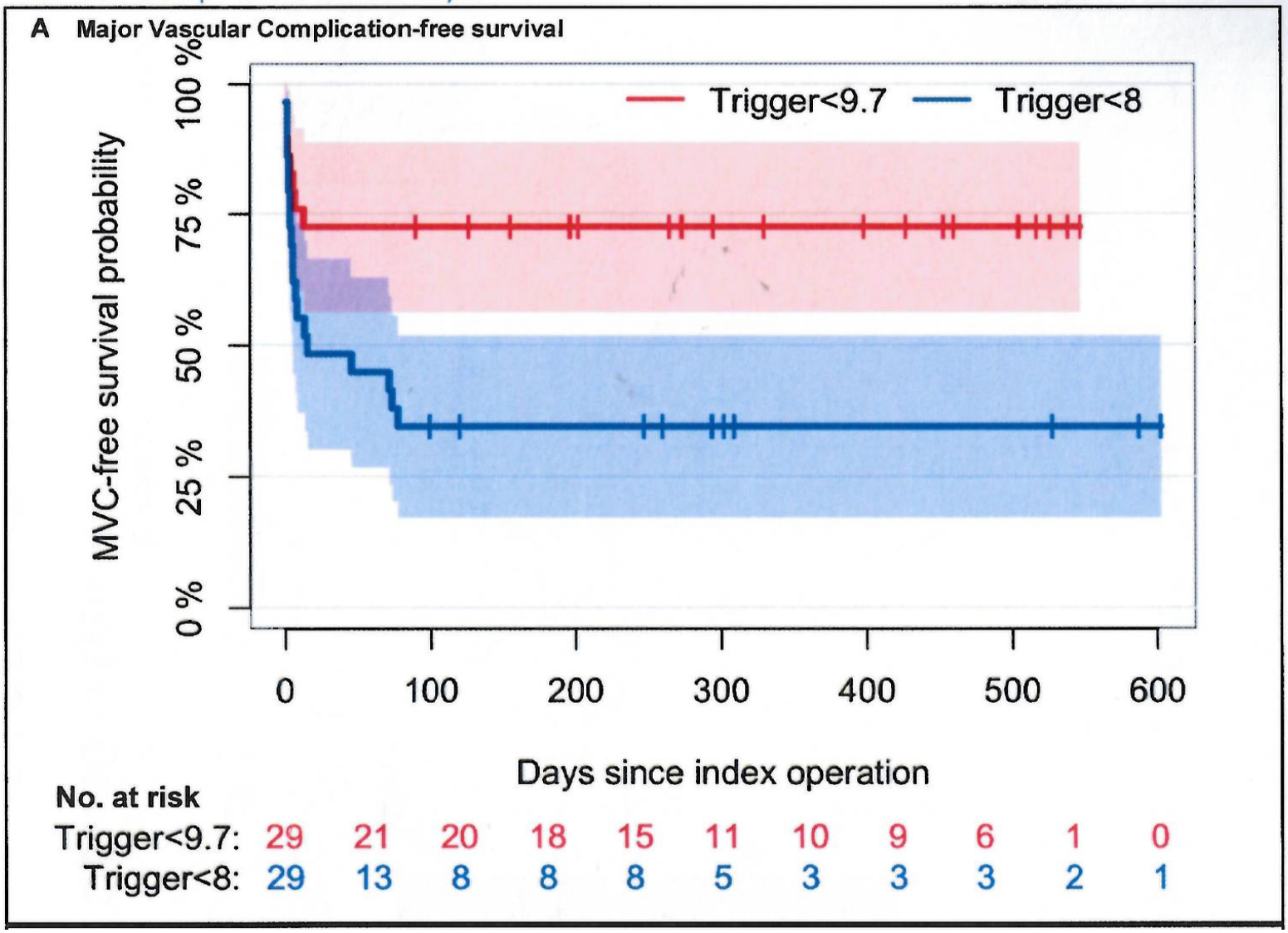
Low vs. high hemoglobin trigger for Transfusion in Vascular surgery (TV): a randomized clinical feasibility trial

Short title: *The Transfusion in Vascular surgery (TV) Trial.*

Anders Møller,[1] Henning B. Nielsen,[2] Jørn Wetterslev,[3] Ole B. Pedersen,[4] Dorthe Hellemann,[1] Per Winkel,[3] Klaus V. Marcussen,[1] Benedicte G.U. Ramsing,[1] Anette Mortensen,[1] Janus C. Jakobsen,[3,4] and Saeid Shahidi[6]

[1]Department of Anesthesia and Intensive care, Slagelse Hospital, Denmark; [2]Sanos Clinic, Herlev, Denmark; [3]Copenhagen Trial Unit, Centre for Clinical Intervention Research, Rigshospitalet, Copenhagen, Denmark; [4]Department of Cardiology, Holbæk Hospital, Denmark, [5]Department of Clinical Immunology, Næstved Hospital, Denmark. [6]Department of General and Vascular Surgery, Slagelse Hospital, Denmark.

Figure 4. Major vascular complication-free survival and Relative Risk of death or Major Vascular Complication at 90 days.




Gewinnung von Blut und Blutbestandteilen (Anzahl und je 100.000 Einwohner). Gliederungsmerkmale: Jahre, Deutschland, Art der Blutspenden
Darstellung: Anzahl
Autologous Blood Donations in Germany
Source: Gesundheitsberichterstattung des Bundes 11.09.2018
Anzahl
224.000
168.000
112.000
56.000
0
2000
2001
2002
2003
2004
2005
2006
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
Eigenblutentnahmen
Die Daten dieser

Clinical Review & Education

JAMA | Special Communication

Patient Blood Management Recommendations From the 2018 Frankfurt Consensus Conference

Markus M. Mueller, MD; Hans Van Remoortel, PhD; Patrick Meybohm, MD, PhD; Kari Aranko, MD, PhD; Cécile Aubron, MD, PhD; Reinhard Burger, PhD; Jeffrey L. Carson, MD, PhD; Klaus Cichutek, PhD; Emmy De Buck, PhD; Dana Devine, PhD; Dean Fergusson, PhD; Gilles Folléa, MD, PhD; Craig French, MB, BS; Kathrine P. Frey, MD; Richard Gammon, MD; Jerrold H. Levy, MD; Michael F. Murphy, MD, MBBS; Yves Ozier, MD; Katerina Pavenski, MD; Cynthia So-Osman, MD, PhD; Pierre Tiberghien, MD, PhD; Jimmy Volmink, DPhil; Jonathan H. Waters, MD; Erica M. Wood, MB, BS; Erhard Seifried, MD, PhD; for the ICC PBM Frankfurt 2018 Group

JAMA. 2019;321(10):983-997. doi:10.1001/jama.2019.0554

JAMA März 2019

Box 2. Research Recommendations

Preoperative Anemia

R1—Since published studies show major differences in the hemoglobin values used for the definition of preoperative anemia, the expert panel recommends to identify optimal hemoglobin thresholds in different patient groups as well as adequate cutoff values.

R2—The expert panel suggests to address the effects of iron supplementation in nonanemic but iron-deficient patients scheduled for major surgery.

R3—The expert panel recommends to investigate the use of short-acting erythropoietins + iron supplementation in adult preoperative patients undergoing elective surgery, with focus on long-term (un)desirable effects, optimal dose, type of surgery (particularly in cancer surgery), copresence of iron deficiency, and cost-effectiveness.

Red Blood Cell (RBC) Concentrate Transfusion Thresholds

R4—The expert panel recommends further research regarding restrictive RBC transfusion thresholds for hemodynamically stable patients with acute upper or lower gastrointestinal tract bleeding. The panel does not recommend further research in hemodynamically unstable patients with acute major bleeding.

R5-9—The expert panel suggests further research on RBC transfusion support in patients with hematologic and oncologic diseases, coronary heart diseases, noncardiac or nonorthopedic surgery, or brain injury.

Rx (no evidence): No further research on hemoglobin thresholds in patients with acute bleeding.

Implementation of Patient Blood Management (PBM) Programs

R10-12—The expert panel suggests further research on the effect of PBM programs on (A) adverse events and patient-important outcomes; (B) compliance, adherence, and acceptability; and (C) cost-effectiveness.

Reproducible definitions and outcome parameters have to be defined beforehand to evaluate the sustainability of PBM programs.

EDITORIAL

Safeguarding the Patient's Own Blood Supply

Michelle P. Zeller, MD; Richard M. Kaufman, MD

"[...]

In this issue of *JAMA*, Mueller and colleagues[6] provide an international PBM guideline based on the 2018 Frankfurt Consensus Conference. The guideline offers evidence-based recommendations on 3 topics: managing preoperative anemia, set-

[...]

future studies will undoubtedly fill in many of the gaps. The PBM guideline, however, creates a solid and important clinical foundation for current practice."

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