Aktuelles aus der Intensivmedizin

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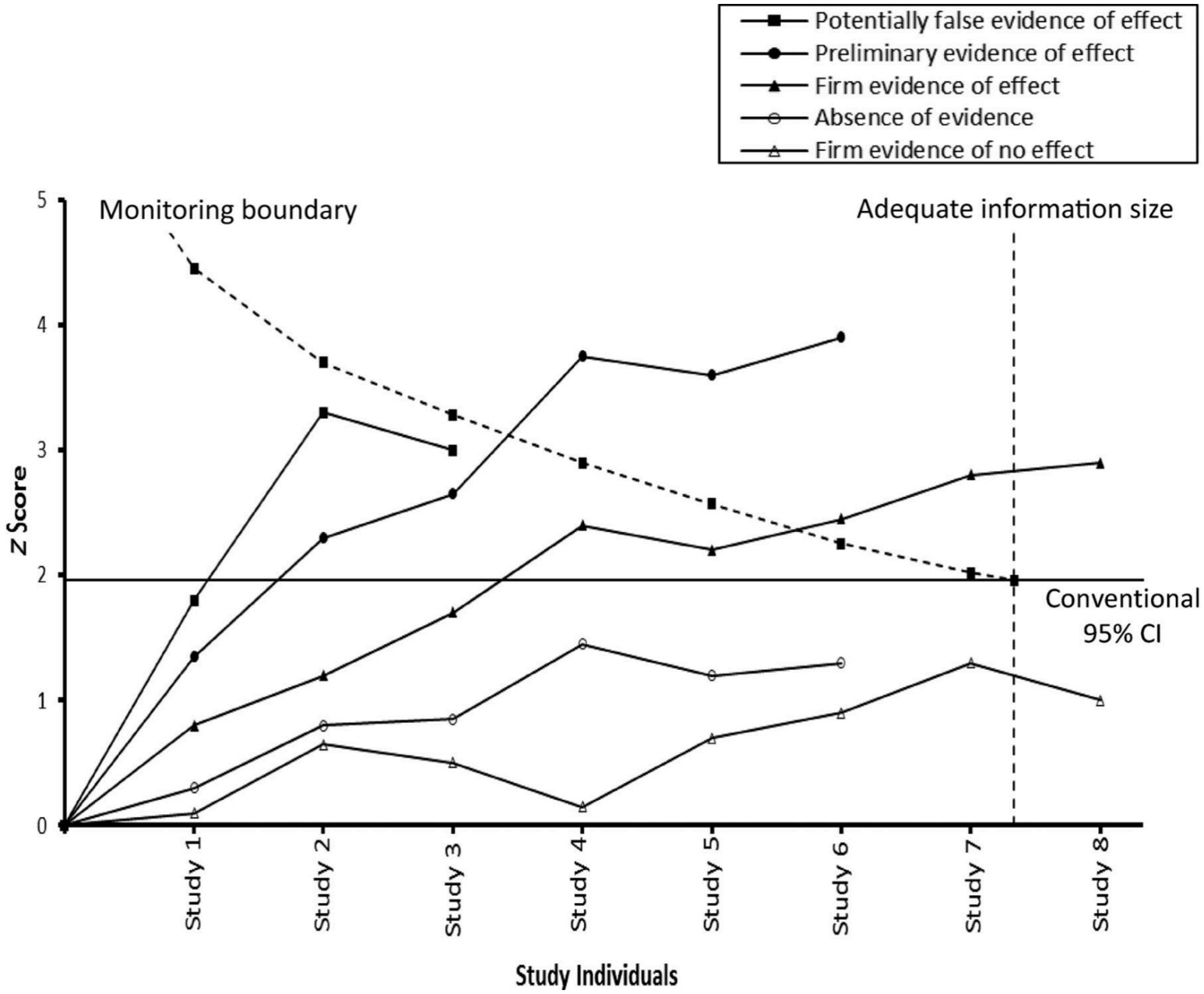
ZIW, Engelberg 2018

Einige wichtige Studien in der Intensivmedizin

1. **The Acute Respiratory Distress Syndrome Network. Ventilation with Lower Tidal Volumes as Compared with Traditional Tidal Volumes for Acute Lung Injury and the Acute Respiratory Distress Syndrome. N Engl J Med 2000; 342:1301-1308**
   - In a randomized controlled trial of 861 patients with ARDS, mechanical ventilation with a tidal volume of 6 ml/kg and plateau pressure ≤ 30 cmH_20, in comparison with tidal volume of 12 ml/kg and plateau pressure ≤ 50cm H_20, was associated with a 9% absolute mortality decrease (31% vs 40%, P=0.007; NNT=11) and a 2 day increase in ventilator-free days (12±11 vs. 10±11; P=0.007).
2. **Finfer. A comparison of albumin and saline for fluid resuscitation in the intensive care unit. N Engl J Med 2004;350(22):2247-56**
   - In a multicenter, randomized, double-blind trial comparing 0.9% saline or 4% albumin for fluid resuscitation in 6997 critically ill patients in the ICU, there was no difference in mortality (729 v 726, RR 0.99; 95 CI 0.91 to 1.09; P=0.87), new single-organ and multiple-organ failure (P=0.85), mean (SD) numbers of ICU days (6.2±6.2 v 6.5±6.6, P=0.44), hospital days (15.6±9.6 v 15.3±9.6; P=0.30), days of mechanical ventilation (4.3±5.7 v 4.5±6.1; P=0.74), or days of renal-replacement therapy (0.4±2.0 v 0.5±2.3) respectively.
3. **Hebert. A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. N Engl J Med 1999;340:409-17**
   - In a randomized controlled trial comparing a red cell transfusion trigger of 7 g/dL versus 10 g/dl in 838 critically ill resuscitated patient, there was no difference in either total 30 day mortality (18.7% vs 23.3%, P=0.11, respectively) or mortality in those with clinically significant cardiac disease (20.5% vs 22.9%; P=0.69). The restrictive transfusion policy was superior for mortality outcome in patients with APACHE II scores of <20 (8.7% vs 16.1%;P=0.03), in patients < 55 years of age (5.7% vs 13.0%; P=0.02), and during hospitalization (22.2% vs 28.1%;P=0.05).
4. **Myburgh. Hydroxyethyl Starch or Saline for Fluid Resuscitation in Intensive Care (CHEST study). NEJM 2012;367:1901-1911**
   - In a blinded randomized controlled trial comparing 6% hydroxyethyl starch 130/0.42 (Voluven) with 0.9% saline for fluid resuscitation in 7000 critically ill patients, this colloid therapy was associated with a 21% increased risk of the requirement for renal replacement therapy (HES RRT requirement 7.0% versus saline 5.8%; relative risk 1.21; 95% CI 1.00 to 1.45; P=0.04 and no mortality benefit (HES mortality 18.0% versus saline mortality 17.0%; relative risk in the HES group, 1.06; 95% CI 0.96 to 1.18; P=0.26). Starch therapy was also associated with increased rates of hepatic failure, rash and pruritus.
5. **Perner. Hydroxyethyl Starch 130/0.4 versus Ringer's Acetate in Severe Sepsis. (6S Trial). N Eng J Med 2012;367:124-134**
   - In a blinded randomized controlled trial comparing 6% hydroxyethyl starch 130/0.42 (Tetraspan) with Ringers acetate for fluid resuscitation in 804 patients with severe sepsis, at 90 days the use of HES was associated with an 8% absolute increase in mortality (51% v 43%; relative risk: 1.17; 95% CI: 1.01 to 1.36; P=0.03) and a 6% absolute increase in renal replacement therapy (22% v 16%; relative risk: 1.35; 95% CI 1.01 to 1.80; P=0.04).
6. **Kress. Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. N Engl J Med 2000;342:1471-7**
   - In a single centre, randomised, controlled trial comparing daily sedation hold with continuous sedation in 128 critically ill mechanically ventilated adults, sedation hold decreased the median durations of mechanical ventilation (4.9 days versus 7.3, p=0.004) and ICU length of stay (6.4 days versus 9.9 days, p = 0.02) as well as the requirement for diagnostic testing for changes in mental status (9% versus 27%, p = 0.02). There were no significant differences in adverse events, including self extubation (intervention group 4% versus control group 7 %, p = 0.88).
7. **NICE-SUGAR Study Investigators. Intensive versus Conventional Glucose Control in Critically Ill Patients. N Engl J Med 2009;360:1283-97**
   - In a multicentre, randomized controlled trial comparing intensive glucose control (81-108 mg/dL / 4.5-6.0 mmol/L) with conventional glucose control (≤180 mg/dL / ≤ 10.0 mmol/L) in 6,104 adult medical and surgical patients, intensive glucose control increased mortality (27.5% vs 24.9%; odds ratio 1.14; 95% CI 1.02 to 1.28; P=0.02). There was no significant difference between medical and surgical patients (odds ratio 1.31 and 1.07 respectively; P=0.10). Severe hypoglycaemic episodes (blood glucose level ≤40mg/dL / 2.2 mmol/L) were more common in the intensive glucose control group (6.8% vs 0.5%; P<0.001). There were no significant differences in the median number of days of mechanical ventilation (P=0.56) or renal-replacement therapy (P=0.39), or days in ICU (P=0.84) or hospital (P=0.86).
8. **Bellomo. Low-dose dopamine in patients with early renal dysfunction: a placebo-controlled randomised trial. Australian and New Zealand Intensive Care Society (ANZICS) Clinical Trials Group. Lancet 2000;356:2139-43**
   - In a multicentre, randomised, controlled, double-blind study comparing low-dose dopamine (2µg/kg/min) infusion with placebo in 328 patients with at least two SIRS criteria and early renal dysfunction, there were no differences in peak serum creatinine concentration (dopamine 245 vs placebo 249 µmol/L; p=0·93), increase in serum creatinine from baseline to highest value (62 vs 66 µmol/L; p=0·82), patients whose serum creatinine concentration exceeded 300 µmol/L (56 vs 56; p=0·92), requirement for renal replacement therapy (35 vs 40; p=0·55), duration of ICU stay (13 vs 14 days; p=0·67), duration of hospital stay (29 vs 33 days; p=0·29), or mortality (69 deaths versus 66 deaths).
9. **Nielsen. Targeted Temperature Management at 33°C versus 36°C after Cardiac Arrest. N Engl J Med 2013;369:2197-2206**
   - In a multicenter, randomized, control trial, comparing temperature management at 33°C with 36°C in 939 comatose patients after out-of-hospital cardiac arrest of presumed cardiac cause, there was no difference in mortality at the end of the trial (33°C group 50% vs 36°C group 48%; hazard ratio with 33°C, 1.06; 95% CI 0.89 to 1.28; P = 0.51), 180-day composite of mortality and poor neurological function (54% vs. 52%, respectively; RR 1.02; 95% CI 0.88 to 1.16; P = 0.78), or serious adverse events (93% vs. 90%, respectively; RR 1.03; 95% CI 1.00 to 1.08; P = 0.09).
10. **Prasad. A Decade of Reversal: An Analysis of 146 Contradicted Medical Practices. Mayo Clinic Proceedings 2013;88(8):790-798**
    - Prasad et al reviewed 2,044 original articles published from 2001 to 2010 in the New England Journal of Medicine, and found of 1,344 articles which investigated a medical practice, 73.0% examined a new medical practice, and 27.0% tested an established practice; while 70.5% had positive findings, and 29.5% had negative findings. Of the 1,344 articles addressing a medical practice, 56% demonstrated a new practice surpassed a standard of care, 12% demonstrated a new practice was no better than current practice, 11% showed an existing practice was no better than a lesser therapy, 10% showed an existing practice was better than a lesser standard, while 10% were inconclusive. Of the 363 articles testing standard of care, 146 (40.2%) reversed that practice, whereas 138 (38.0%) reaffirmed it.
11. **Sprung. Hydrocortisone Therapy for Patients with Septic Shock. N Engl J Med 2008;358:111-124**
    - In a multicentre, double-blind, randomized placebo-controlled trial comparing hydrocortisone (50mg IV 6 hourly, then tapered) with placebo in 499 patients with septic shock, there was no significant difference in 28-day mortality (hydrocortisone group 34.3% vs placebo group 31.5%; P=0.51). Subgroup analyses of 28-day mortality based on response to corticotropin also showed no difference between study groups. Hydrocortisone hastened reversal of shock compared to placebo, however, with more episodes of superinfection, including new sepsis and septic shock.
12. **Guérin. Prone Positioning in Severe Acute Respiratory Distress Syndrome (PROSEVA). New Engl J Med 2013; 368:2159-2168**
    - In a multicentre, randomised control trial, comparing prolonged periods of prone position ventilation with ongoing supine position ventilation, in 466 patients with moderate-to-severe ARDS, prone positioning was associated with reduced 28 day mortality (16% versus 32.8%, hazard ratio 0.39, 95% CI 0.25 to 0.63, P<0.001), reduced 90 day mortality (23.6% versus 41%, HR 0.44, 95% CI 0.29 to 0.67, P<0.001), and less cardiac arrests (31 patients versus 16 patients, P=0.02), with no difference in other complications.
13. **de Jonge. Effects of selective decontamination of the digestive tract on mortality and acquisition of resistant bacteria in intensive care: a randomised controlled trial. Lancet 2003;362:1011-1016** *(abstract)*
    - In an unblinded, single center, randomized control trial comparing selective digestive tract decontamination (oral and enteral polymyxin E, tobramycin, and amphotericin B combined with an initial 4-day course of intravenous cefotaxime) with standard treatment in 934 critically ill patients, SDD was associated with reductions in ICU mortality (15% versus 23%, P=0.002), hospital mortality (24% versus 31%, P=0.02) and colonization with resistant gram-negative bacteria (16% versus 26%, P=0.001), with equal colonization of vancomycin resistant enterococcus (1% versus 1% p=1.0) and absence of methicillin resistant staphylococcus aureus colonization.
14. de Smet. Decontamination of the digestive tract and oropharynx in ICU patients. N Engl J Med. 2009 Jan 1;360(1):20-31
15. The ProCESS Investigators. A Randomized Trial of Protocol-Based Care for Early Septic Shock (ProCESS study). New Engl J Med 2014;epublished March 18th
16. **Harvey. Assessment of the clinical effectiveness of pulmonary artery catheters in management of patients in intensive care (PAC-Man): a randomised controlled trial. Lancet 2006;366:472-477** *(abstract)*
    - In a multicenter, randomized control trial comparing critical care management with a pulmonary artery catheter to management without a pulmonary artery catheter in 1,014 general ICU patients, there was no difference in hospital mortality (68% versus 66%,
17. **Maitland. Mortality after Fluid Bolus in African Children with Severe Infection (FEAST Trial). N Engl J Med 2011;364:2483-2495** *(Paediatric Study)*
    - Maitland et al performed a stratified (severe hypotension or not), multicenter, randomized control trial, in a resource-limited setting in sub-Saharan Africa, comparing a fluid bolus (20 to 40 ml of 5% albumin or 0.9% saline) with no fluid bolus at admission to hospital in 3,141 children with febrile illness and impaired perfusion, and found fluid bolus therapy was associated with a higher mortality at 48 hours (albumin 10.6%, saline 10.5%, no bolus 7.3%; relative risk bolus therapy versus no bolus 1.45, 95% CI 1.13 to 1.86, P=0.003), and 28 days (12.2%, 12.0% & 8.7%, respectively; RR bolus therapy versus no bolus p=0.004), with similar incidences of pulmonary oedema, increased intracranial pressure (2.6%, 2.2% versus 1.7% P=0.17), and neurological sequela in the three groups (P=0.92).
18. **Annane. Norepinephrine plus dobutamine versus epinephrine alone for management of septic shock: A randomised trial. Lancet 2007; 370:676-684** *(abstract)*
    - In a blinded, multicenter, randomized control trial, comparing noradrenaline plus dobutamine with adrenaline in 330 patients with septic shock, aiming to maintain mean arterial pressure at 70 mmHg, there were no significant differences in 28 day mortality (34% vs. 40%, relative risk 0.86, 95% CI 0.65 to 1.14, P=0.31), ICU mortality (47%s vs 75, p=0·69), hospital mortality (52% vs 49%, p=0·51), 90 day mortality (52% vs 50%, p=0·73), time to haemodynamic success (p=0·67), time to vasopressor withdrawal (p=0·09), or rates of serious adverse events.
19. **Peek. Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial. Lancet 2009; 374: 1351-63** *(abstract)*
    - In a multicenter, randomized control trial, comparing ongoing conventional mechanical ventilation in a non-ECMO centre with transfer to an ECMO centre for respiratory support with either conventional mechanical ventilation or ECMO in 180 patients with severe hypoxic respiratory failure, ECMO centre management, where only 75% of the transferred patients actually received ECMO, was associated with increased 6-month survival (63% vs. 47%, relative risk 0.69, 95% CI 0.05 to 0.97, P=0.03) and a gain of 0·03 quality-adjusted life-years at 6-months, with a lifetime model predicting the cost per QALY of ECMO to be £19 252 (95% CI 7622—59 200) at a discount rate of 3·5%
20. **Ranieri. Drotrecogin Alfa (Activated) in Adults with Septic Shock (PROWESS-SHOCK Study). N Engl J Med 2012;366:2055-206**
    - In a blinded, multicenter, randomized, control trial, comparing activated protein C (24 µg/kg/hr for 96 hours) with a placebo, in


Potentially false evidence of effect
Preliminary evidence of effect
Firm evidence of effect
Absence of evidence
Firm evidence of no effect
Monitoring boundary
Adequate information size
Conventional
95% CI
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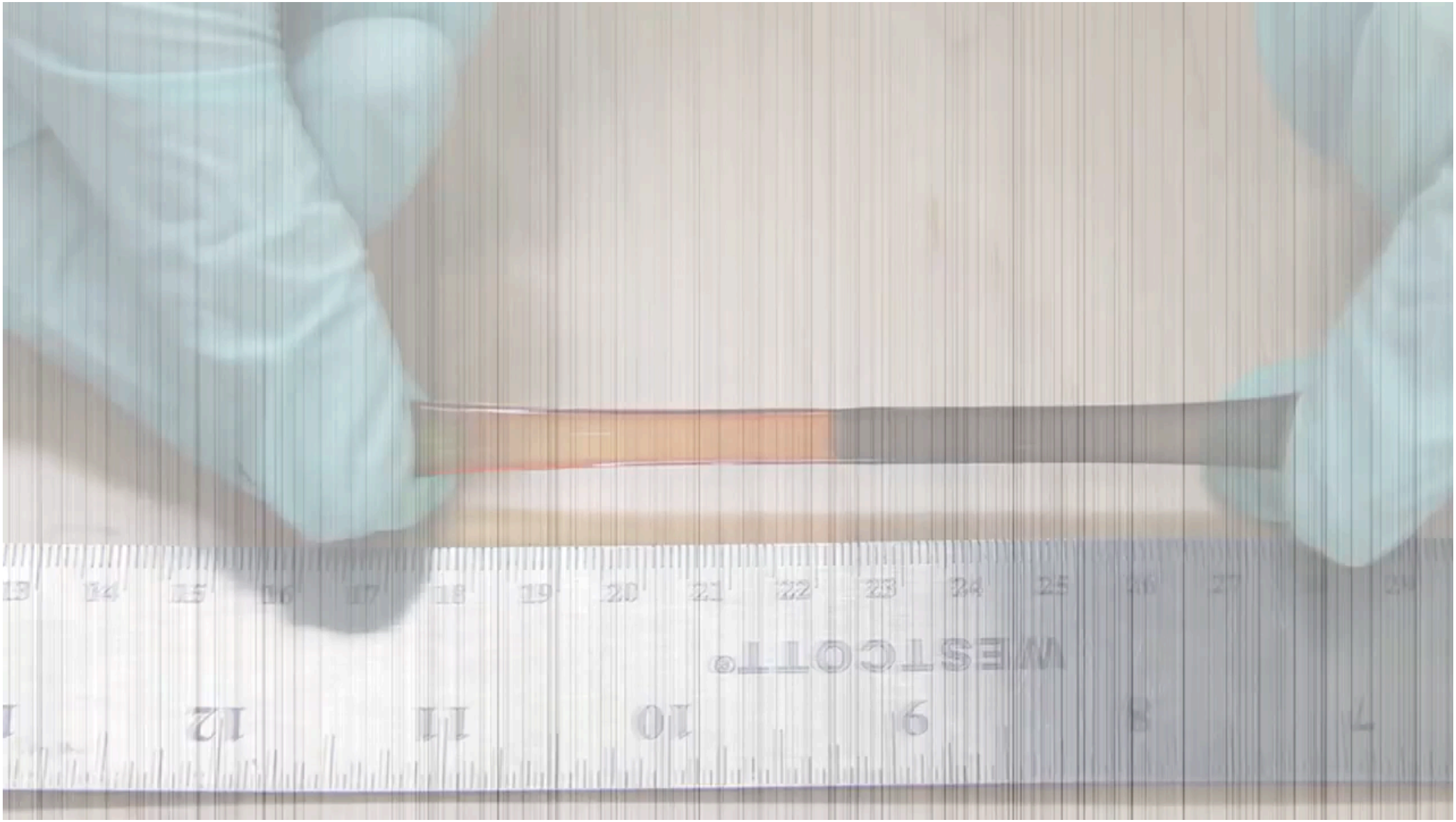
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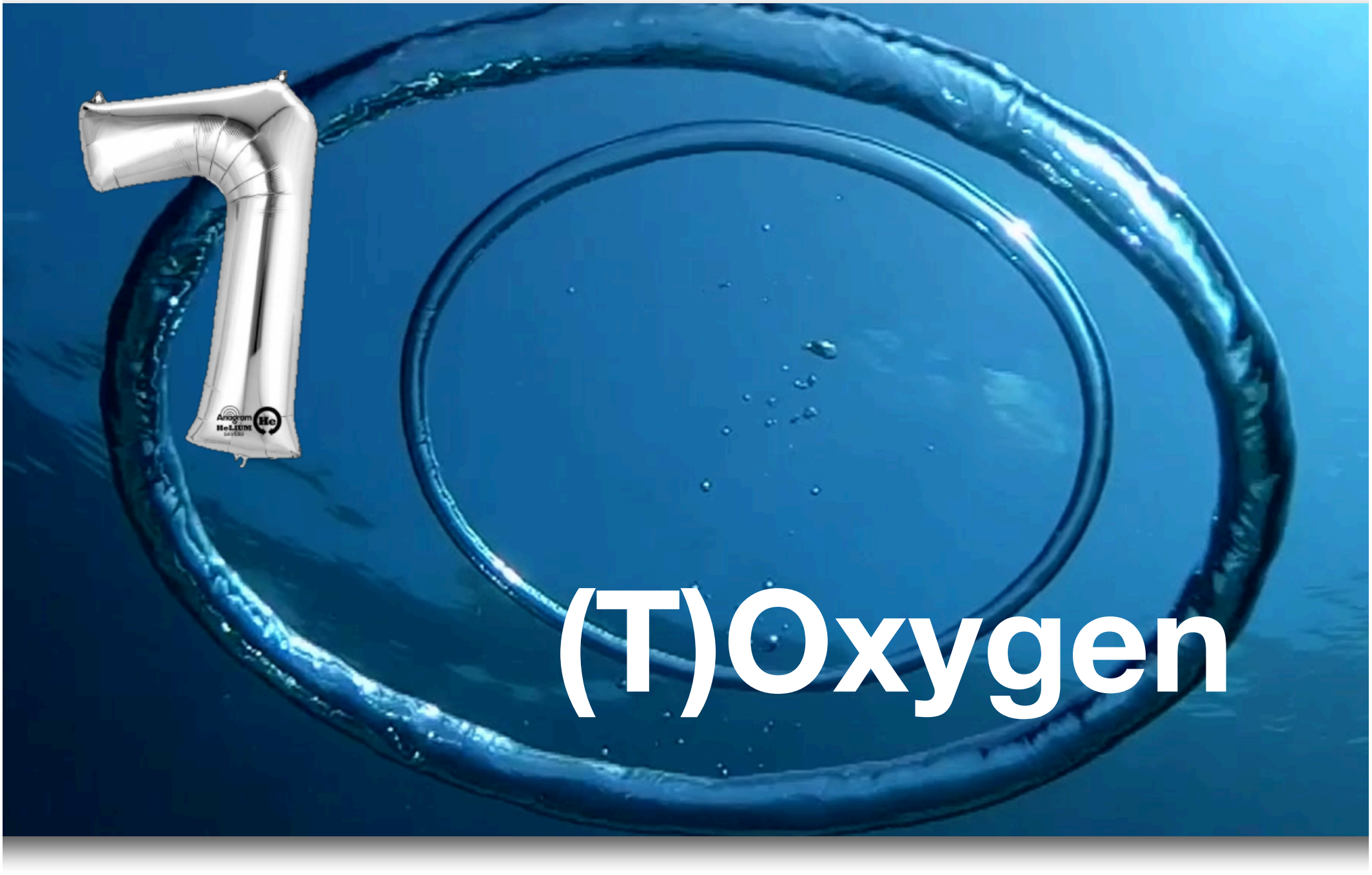
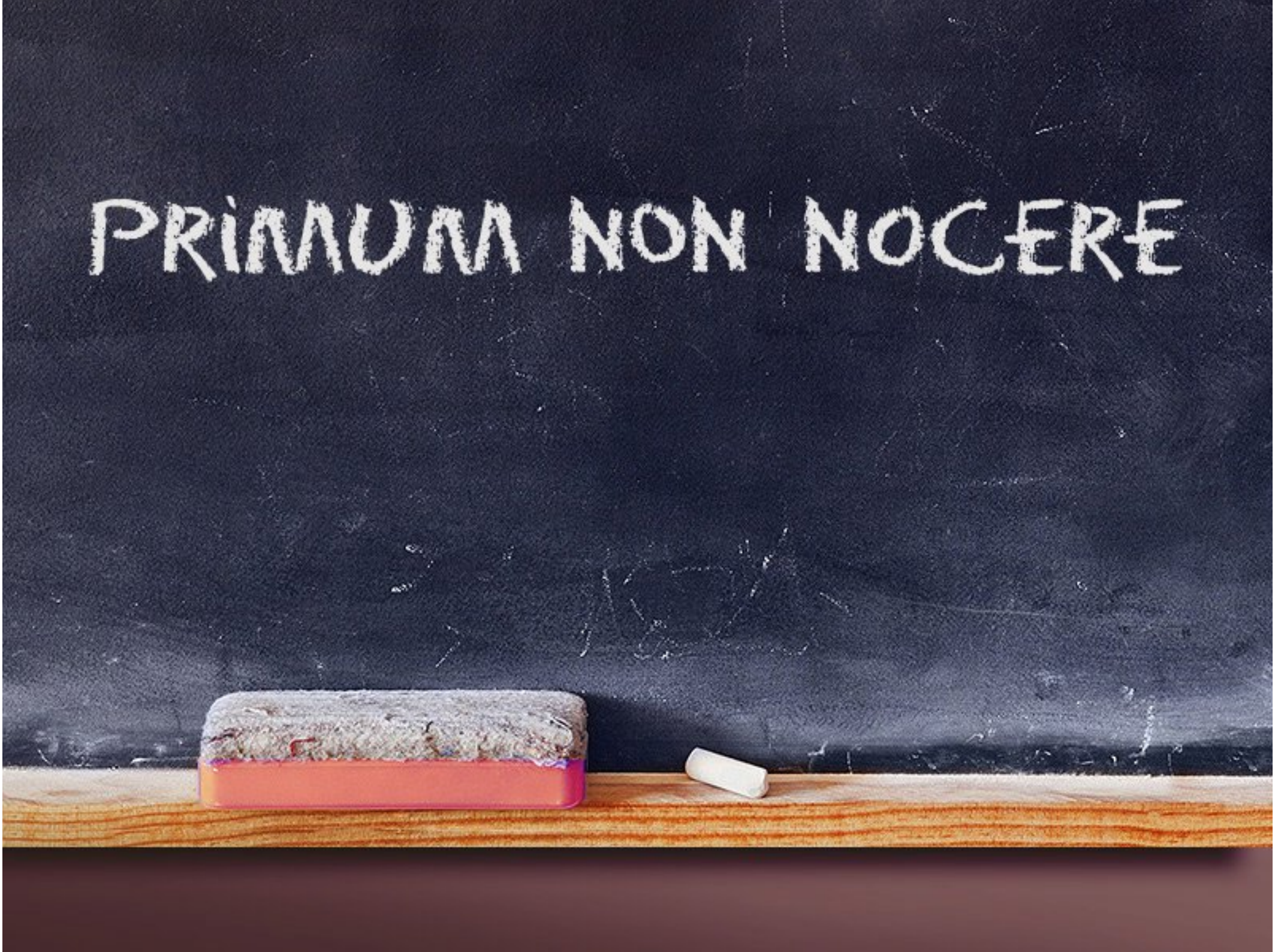
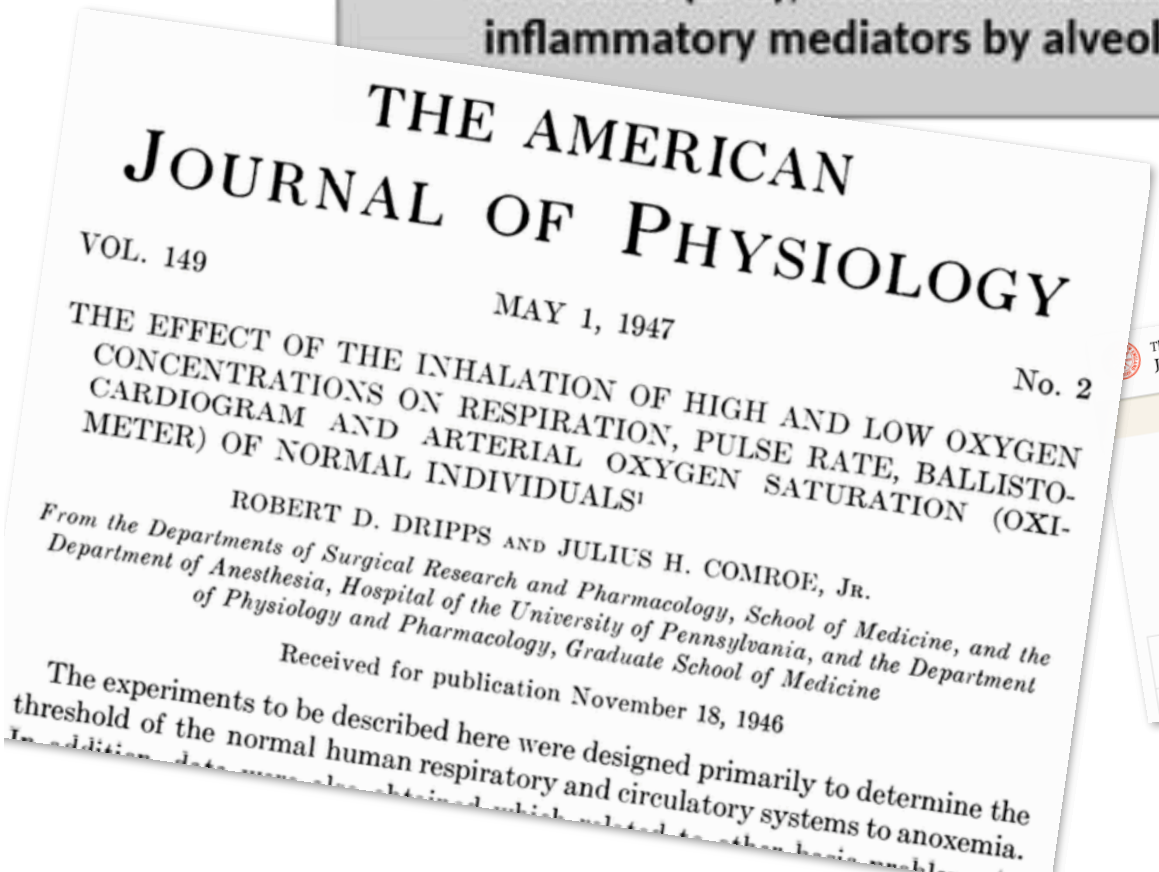

(T)Oxygen


Stroke
Herzinfarkt
Sepsis
Cardiac Arrest
Trauma


PRIMUM NON NOCERE

- 1946, Dripps and Comroe, *Fed Proc*
  - 90 healthy men, FiO_2 of 50-100%, 24h
  - At 100%: Chest pain, reduction of vital capacity in all pts after 14 h
  - At 75%: same finding in 50% of volunteers, after 24h
  - At 50%: no effect
- 1983, Davies et al, *NEJM*
  - 14 healthy men, FiO_2 95%, 17h
  - Alveolitis (BAL), increased albumin permeablity, production of inflammatory mediators by alveolar macrophages



THE AMERICAN JOURNAL OF PHYSIOLOGY

VOL. 149 MAY 1, 1947 No. 2

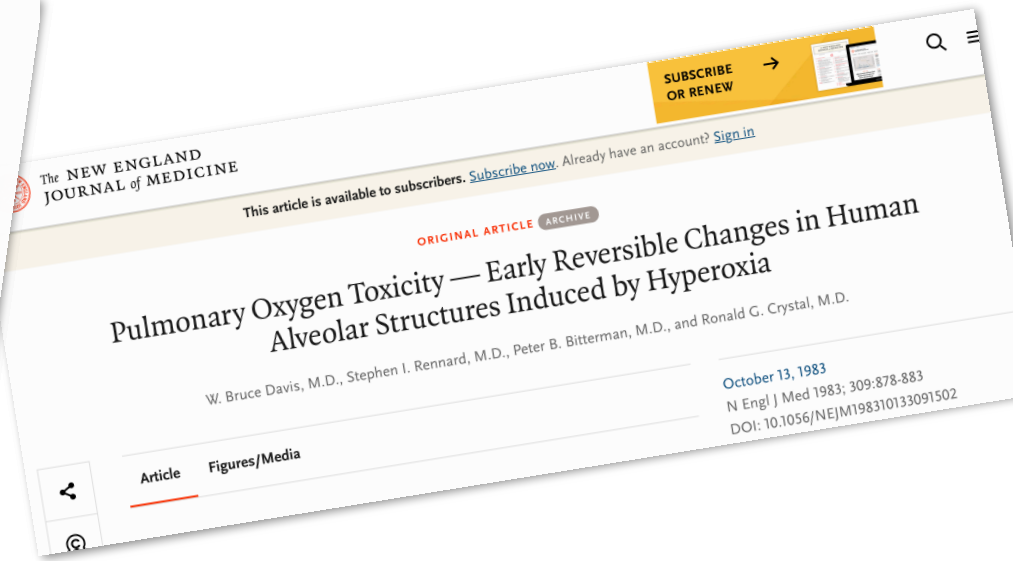
THE EFFECT OF THE INHALATION OF HIGH AND LOW OXYGEN CONCENTRATIONS ON RESPIRATION, PULSE RATE, BALLISTOCARDIOGRAM AND ARTERIAL OXYGEN SATURATION (OXIMETER) OF NORMAL INDIVIDUALS[1]

ROBERT D. DRIPPS AND JULIUS H. COMROE, JR.

From the Departments of Surgical Research and Pharmacology, School of Medicine, and the Department of Anesthesia, Hospital of the University of Pennsylvania, and the Department of Physiology and Pharmacology, Graduate School of Medicine

Received for publication November 18, 1946

The experiments to be described here were designed primarily to determine the threshold of the normal human respiratory and circulatory systems to anoxemia.



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ORIGINAL ARTICLE ARCHIVE

Pulmonary Oxygen Toxicity — Early Reversible Changes in Human Alveolar Structures Induced by Hyperoxia

W. Bruce Davis, M.D., Stephen I. Rennard, M.D., Peter B. Bitterman, M.D., and Ronald G. Crystal, M.D.

October 13, 1983
N Engl J Med 1983; 309:878-883
DOI: 10.1056/NEJM198310133091502

Article Figures/Media

- Hyperoxia seems to **impair left ventricular function**:
  Mak S et al, Chest 2001 Aug;120(2):467-73.
  Haque W et al. J Am Coll Cardiol. 1996 Feb;27(2):353-7.

- The systematic use of supplemental oxygen patients with acute myocardial infarction appears to **increase the risk of death**:
  Cabello JB et al. Cochrane Database Syst Rev. 2013 Aug 21;(8):CD007160

- Hyperoxia is associated with **increased mortality** in patients admitted to the ICU after resuscitation:
  Kilgannon JH, JAMA. 2010 Jun 2;303(21):2165-71

- Mean values of FiO2 and PaO2 in the first 24 hours **directly correlated with mortality** (although it is not clear whether this association is causal or merely a reflection of differences in severity of illness):
  De Jonge et al. Crit Care. 2008;12(6):R156

- Supplemental oxygen in patients with ST-elevation myocardial infarction but without hypoxia seems to increase early myocardial injury and is **associated with larger myocardial infarct size, AVOID Trial**:
  Stub et al. Circulation. 2015 Jun 16;131(24):2143-50.

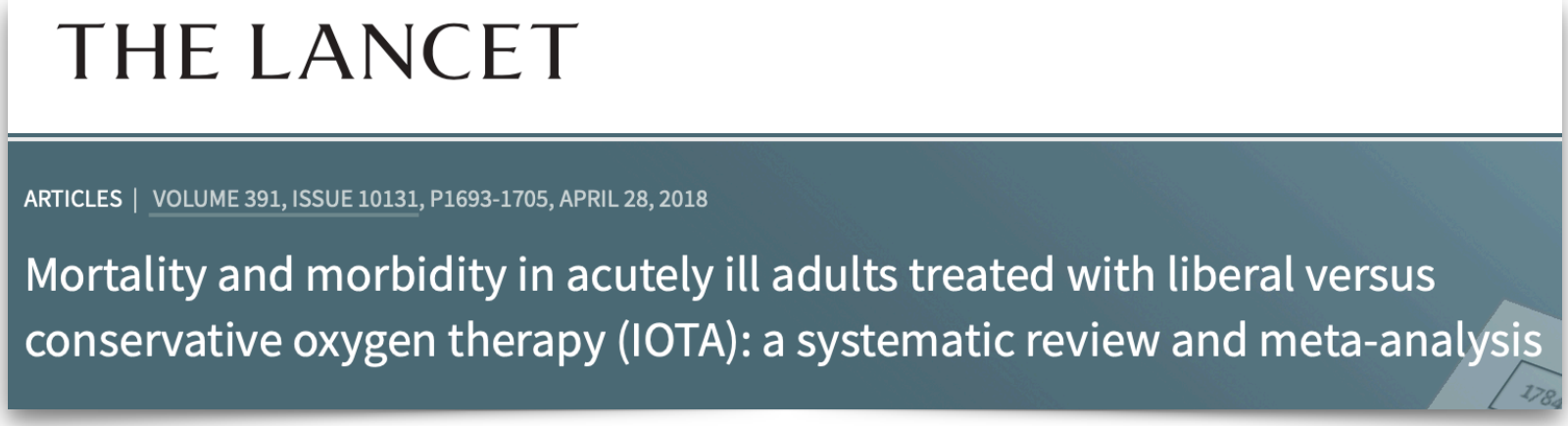
- **DETO2X** zeigte keinen Unterschied in 1-Jahresmortalität zwischen Raumluft und O2-Applikation bei normoxämen AMI-Patienten, N Engl J Med 2017; 377:1240-1249

- **Oxygen-ICU** zeigte eindrücklichen Mortalitätsbenefit bei kritisch kranken Patienten, welche eine konservative O2-Therapie erhielten, *JAMA.* 2016;316(15):1583-1589

The Question Is…

- Erhöht eine liberale O2-Strategie verglichen mit einer konservativen O2-Therapie die Sterblichkeit im Spital?

- Was ist denn die optimale Sauerstoff-Sättigung?



- Systematischer Review und Meta-Analyse
  - Fokussierte klinische Fragestellung
  - Kriterien der eingeschl. Studien mit hohem Standard
  - Ähnliche Resultate in den meisten Studien
- Insgesamt 25 Trials mit > 16’000 Patienten
- Medium Follow up 3 Mte (2-6 Mte)
- Risk of bias in 18 Trials als ‘LOW’ eingestuft

THE LANCET

ARTICLES | VOLUME 391, ISSUE 10131, P1693-1705, APRIL 28, 2018

Mortality and morbidity in acutely ill adults treated with liberal versus conservative oxygen therapy (IOTA): a systematic review and meta-analysis

Liberale O2-Gabe

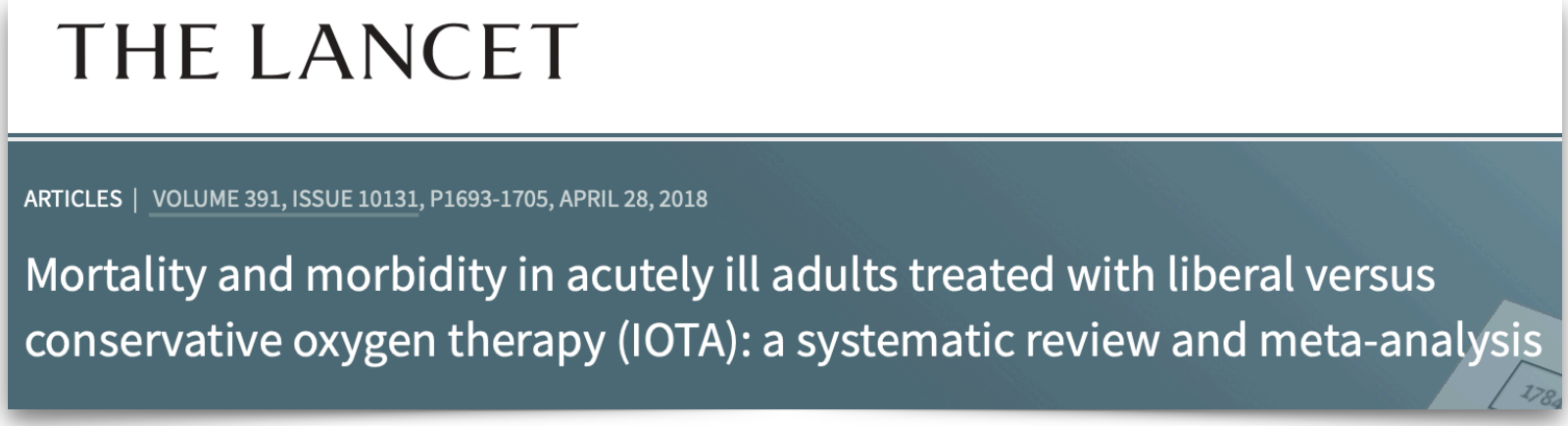
Im Median FiO2 von 0,52 während 8 Stunden

Versus

Conservative O2-Gabe

Raumluft

Beides wurde über Nasensonden (4), Face-Masks (13) oder Inv. Ventilation (8) verabreicht



Bei höheren SpO2 Werten war die liberale O2-Therapie mit einer höheren relative risk Mortalität verbunden (14 randomisiert-kontrollierte Studien, High Quality Data)

Subgruppen-Analyse: Resultate gleich, ob bei IPS- oder nicht-IPS-Patienten

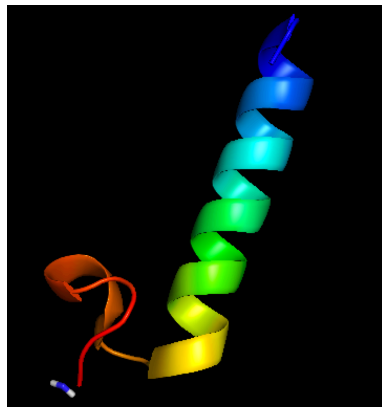
- **Es besteht gute Evidenz:**
  - **Hyperoxie ist lebensgefährlich**
  - **Liberale O2-Therapie ist bei kritisch kranken Patienten nicht von Vorteil**

- **Take Home: Bei SpO2-Werten >94-96% O2-Gabe reduzieren/ stoppen!**

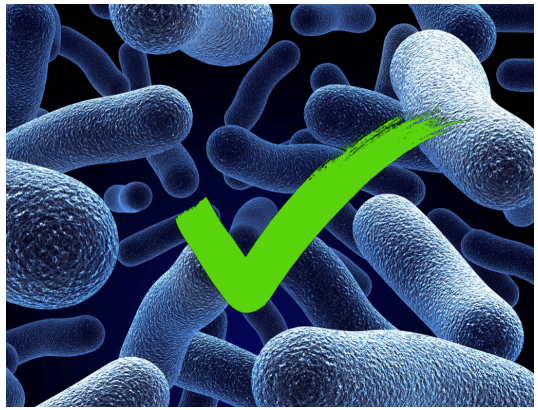

Anti-Calcitonin?
6

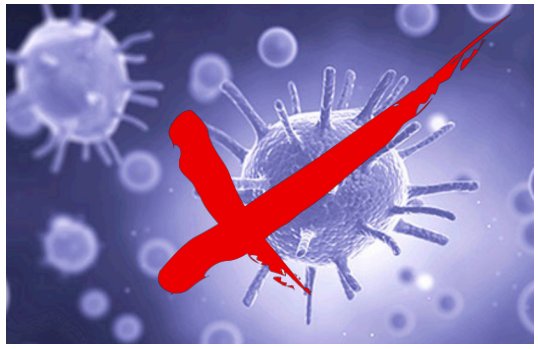
STOP THE OVERUSE OF ANTIBIOTICS

Procalcitonin

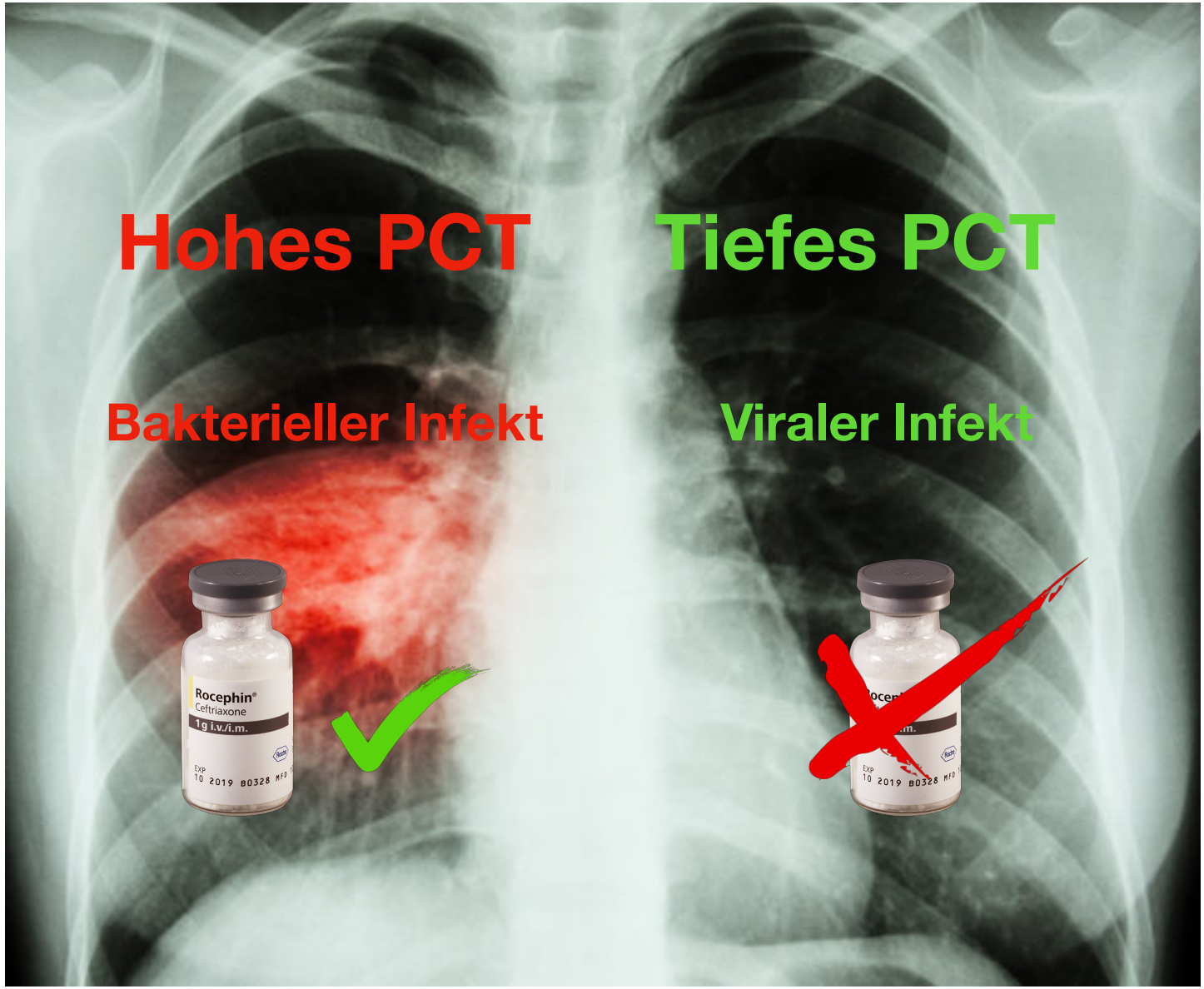


- Ein Akut-Phasen-Peptide (ähnlich zum CRP)
- Normalerweise kaum nachweisbar
- Steigt bei inflammatorischem Stimulus an, v.a. bei bakteriellen Infekten
- Kaum bei viralen Infekten





Lower Respiratory Tract Infections LRTI's

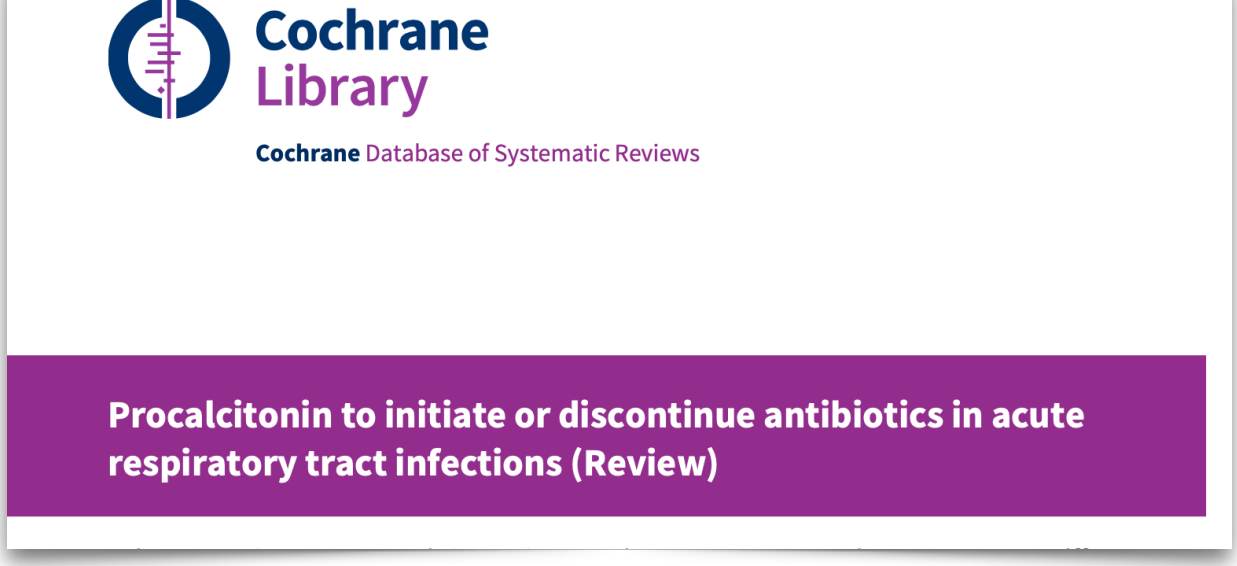


ThermoFisher SCIENTIFIC

B·R·A·H·M·S PCT (Procalcitonin) supports responsible use of antibiotics

Due to its high sensitivity and specificity B·R·A·H·M·S PCT safely supports responsible use of antibiotics to prolong their effectiveness. Strong evidence supports the reduction of antibiotics using PCT-guided antibiotic stewardship protocols. PCT guidance could help reduce the initial antibiotic prescription rates and also the antibiotic treatment duration.

Surviving Sepsis Campaign: "We suggest that measurement of procalcitonin levels can be used to support shortening the duration of antimicrobial therapy in sepsis patients." *Source: International Guidelines for Management of Sepsis and Septic Shock, 2016*



- 26 Trials, 6700 Patienten
- Potential für einen PCT-Approach
- Aber:
    - Meiste Trials mit eher wenig Patientenzahlen
    - Evidenz bei Notfallstationen minimal
    - Im outpatient-setting keine Mortalitäts-Differenz
    - Conflicts of interest

PS, MC-C, and BM have received support from Thermo-Fisher and bioMérieux to attend meetings and fulfilled speaking engagements. BM has served as a consultant for and received research support from Thermo-Fisher. HCB and MB have received research support from Thermo-Fisher for a previous meta-analysis regarding procalcitonin. DWdL's hospital received financial support for the randomisation tool by ThermoFisher. DS, OB, and MT have received research support from Thermo-Fisher. TW and SS have received lecture fees and research support from Thermo-Fisher. CEL has received lecture fees from Brahms and Merck Sharp & Dohme-Chibret. JC has received consulting and lecture fees from P zer, Brahms, Wyeth, Johnson & Johnson, Nektar-Bayer, and Arpida. MW has received consulting and lectures fees from Merck Sharp & Dohme-Chibret, Janssen Cilag, Gilead, Astellas, Sano , and Thermo-Fisher. FT's institution received funds from Brahms. CC has received an unrestricted grant of €2000 from Thermo-Fisher Scientific, and non-fiancial support from bioMérieux for the ProToCOLD study. YS has received unrestricted research grants from Thermo-Fisher, bioMérieux, Orion Pharma, and Pfizer. ARF has served on advisory boards for Novavax, Hologic, Gilead, and MedImmune; and has received research funding from AstraZeneca, Sanofi Pasteur, GlaxoSmithKline, and ADMA Biologics. J-USJ declares that he was invited to the European Respiratory Society meeting 2016 by Roche Pharmaceuticals.

Critical Care Medicine. 46(5):684–690, MAY 2018
DOI: 10.1097/CCM.0000000000002953,
PMID: 29293146
Issn Print: 0090-3493
Publication Date: 2018/05/01

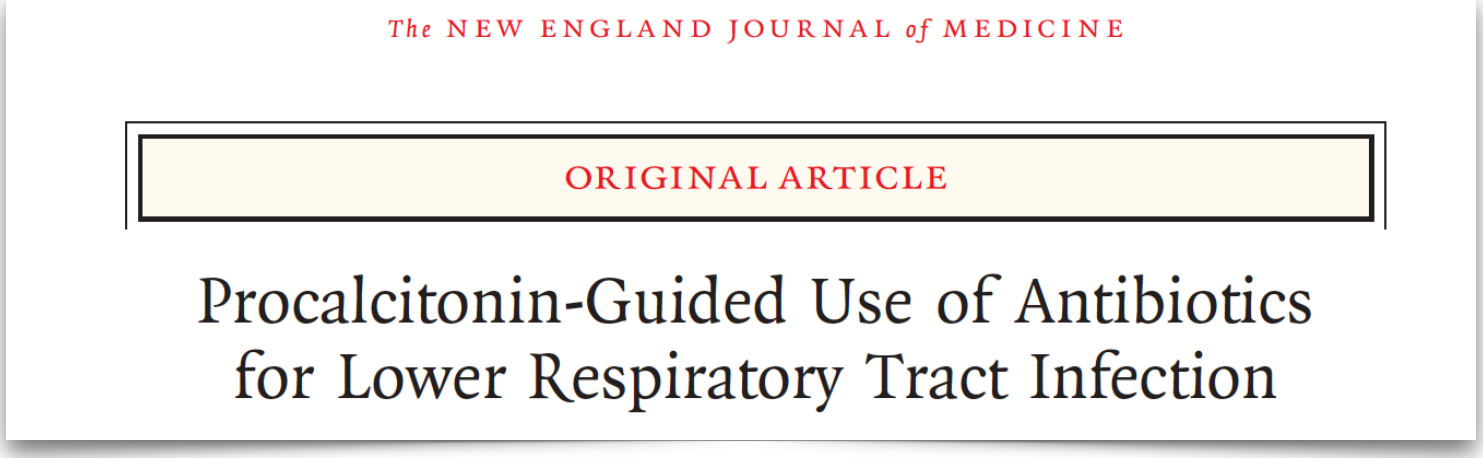
Print

Systematic Review and Meta-Analysis of Procalcitonin-Guidance Versus Usual Care for Antimicrobial Management in Critically Ill Patients: Focus on Subgroups Based on Antibiotic Initiation, Cessation, or Mixed Strategies*

- **Meta-Analyse** von 2018 (15 Trials, >6000 Pat.):
  - PCT-guided Antibiotika-Therapiebeginn bei IPS-Patienten: **keine** Verbesserung der Mortalität in 30 Tagen
  - Aber: PCT-guided Absetzen von Antibiotika: tiefere Mortalität

The Question Is…

- Führt ein Procalcitonin-guided Approach zu einem reduzierten Antibiotika-Verbrauch innert 30 Tagen?

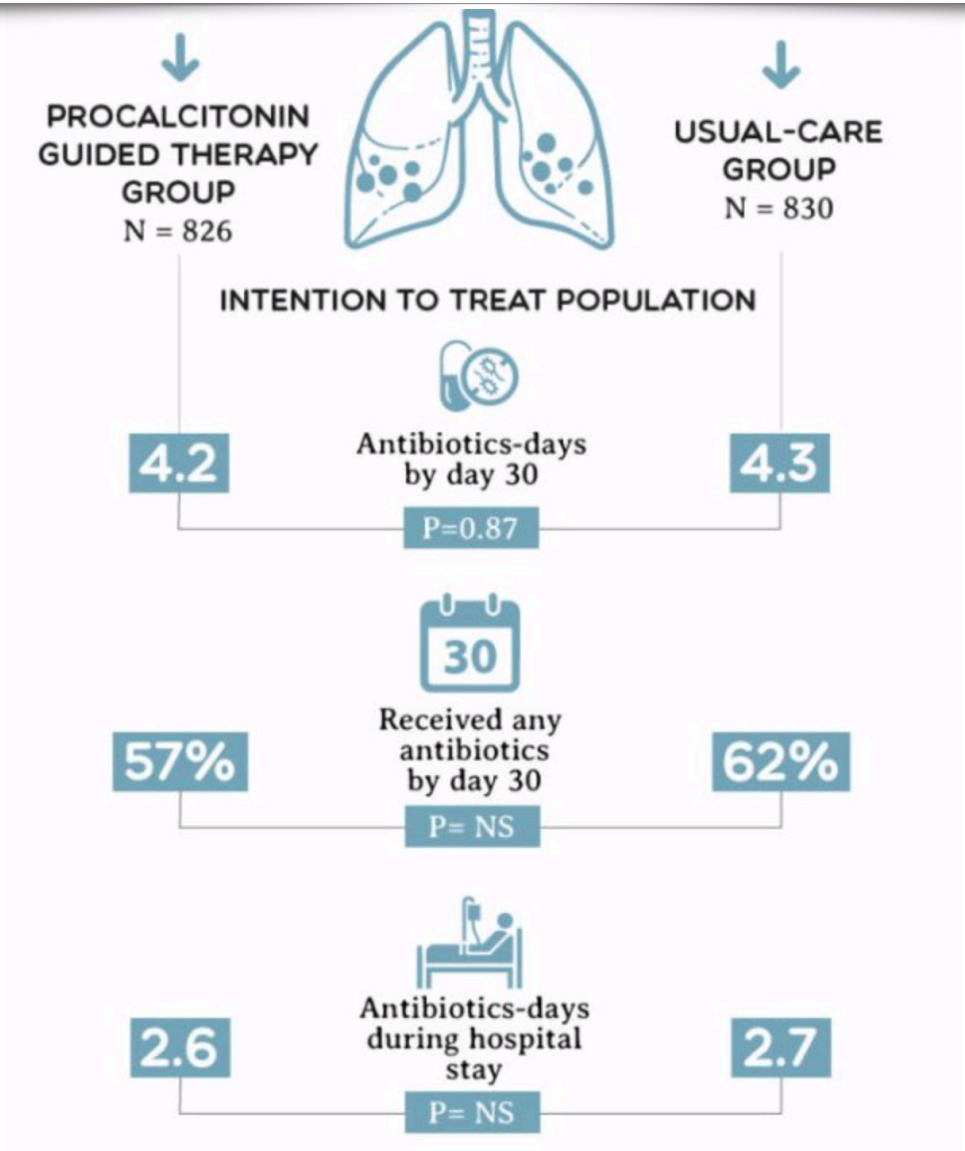


- Multicenter, randomisiert Studie an 14 Notfallstationen in den US
- 1656 Pat. mit Diagnose Pneumonie eingeschlossen
- Randomisiert: Standard Care vs PCT-guided Care

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Procalcitonin-Guided Use of Antibiotics for Lower Respiratory Tract Infection



Auch kein Unterschied bezüglich Adverse Outcomes

- **Procalcitonin als isolierter Marker bezüglich Beginn einer antibiotischen Therapie: Der Beweis steht noch aus!**

- **Procalcitonin ist wahrscheinlich nicht besser als eine gute klinische Beurteilung (?)**

- **Take Home: Vor allem Hilfreich bei der Frage nach Absetzen einer antibiotischen Therapie!**

Topical Tranexamic Acid

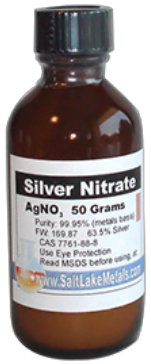
- Epistaxis ist häufig
- Lifetime Incidence 60%

ELSEVIER
Otolaryngologic Clinics of North America
Volume 41, Issue 3, June 2008, Pages 525-536

Epistaxis

Thomas O. Gifford MD (Capt, MC, USAF) [a], Richard R. Orlandi MD, FACS [a, b, c]

- Standard Therapie:

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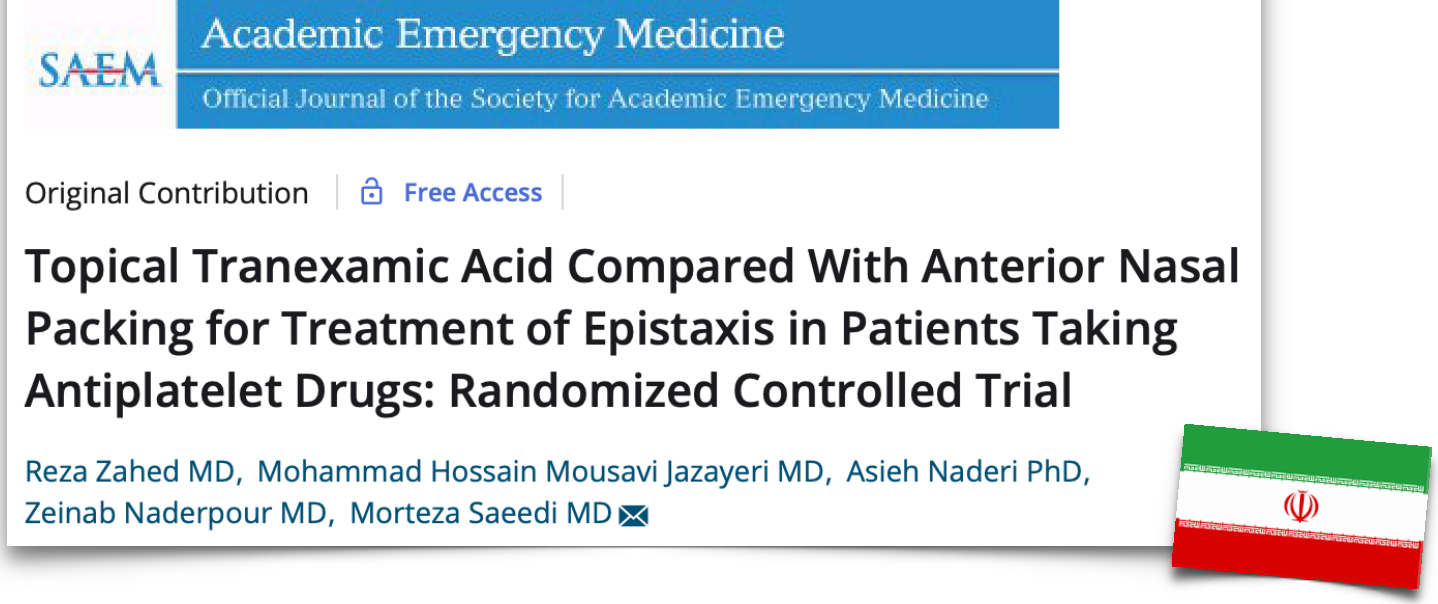
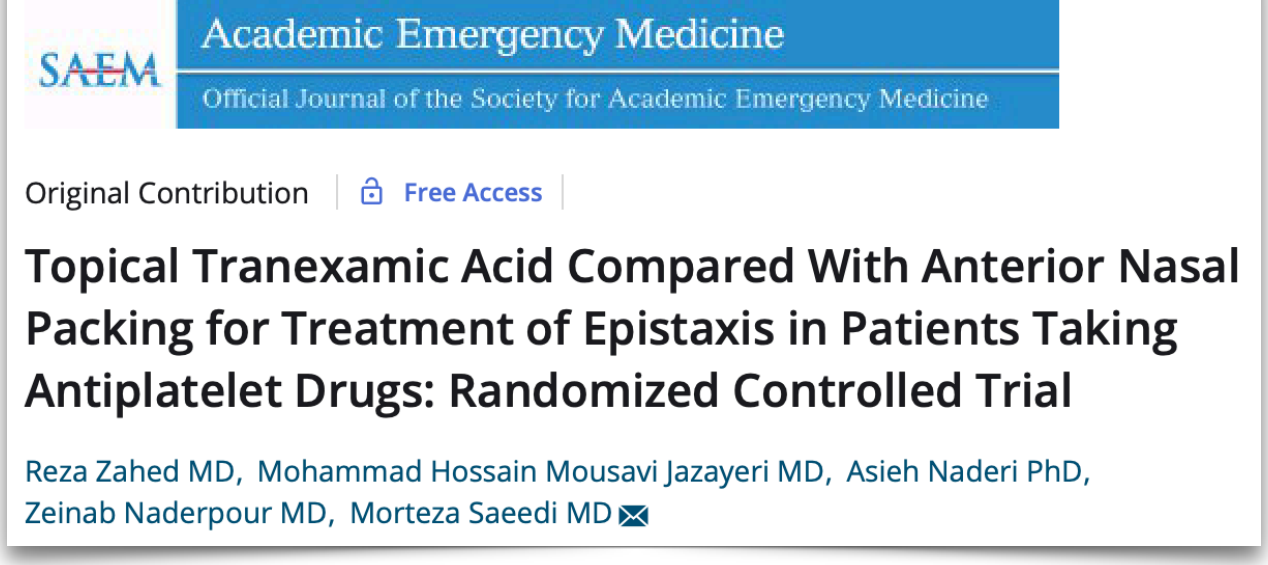


- Randomisiert, kontrollierte Studie
- Vergleich: Nasentamponade vs TXA bei Patienten mit Thrombozytenaggregationshemmer (124 Pat.)
- Primärer Endpoint: Blutstillung nach 10 Minuten
- Sekundäre Endpunkte: nach 24h, 1 Woche, Zufriedenheit



SAEM
Academic Emergency Medicine
Official Journal of the Society for Academic Emergency Medicine

Original Contribution | Free Access

Topical Tranexamic Acid Compared With Anterior Nasal Packing for Treatment of Epistaxis in Patients Taking Antiplatelet Drugs: Randomized Controlled Trial

Reza Zahed MD, Mohammad Hossain Mousavi Jazayeri MD, Asieh Naderi PhD, Zeinab Naderpour MD, Morteza Saeedi MD

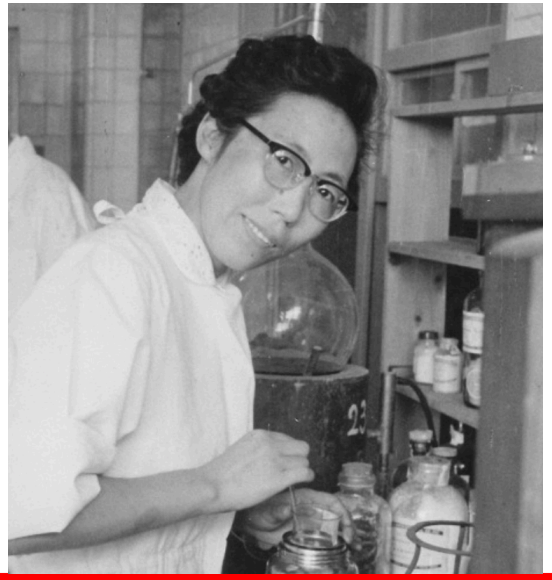
	Anterior Pack	Topical TXA	Difference
Cessation of Bleeding at 10 Min (Primary Outcome)	29%	73%	44% (26 - 57) NNT ≈ 2
Epistaxis Recurrence 24 Hrs (Secondary Outcome)	10%	5%	-5% (-15 - 5)
Epistaxis Recurrence 1 Week (Secondary Outcome)	21%	5%	-16% (-28 - -4)
ED LOS - Discharge <2Hrs (Secondary Outcome)	13%	97%	84% (71 - 91)
Patient Satisfaction 0 - 10 (Secondary Outcomes)	Median = 4	Median = 9	---

- **Topische TXA ist eine sichere, effiziente und rasche Behandlungsoption bei vorderer Epistaxis**

- **Definitiv immer ein Versuch wert!**

1-2 Franken

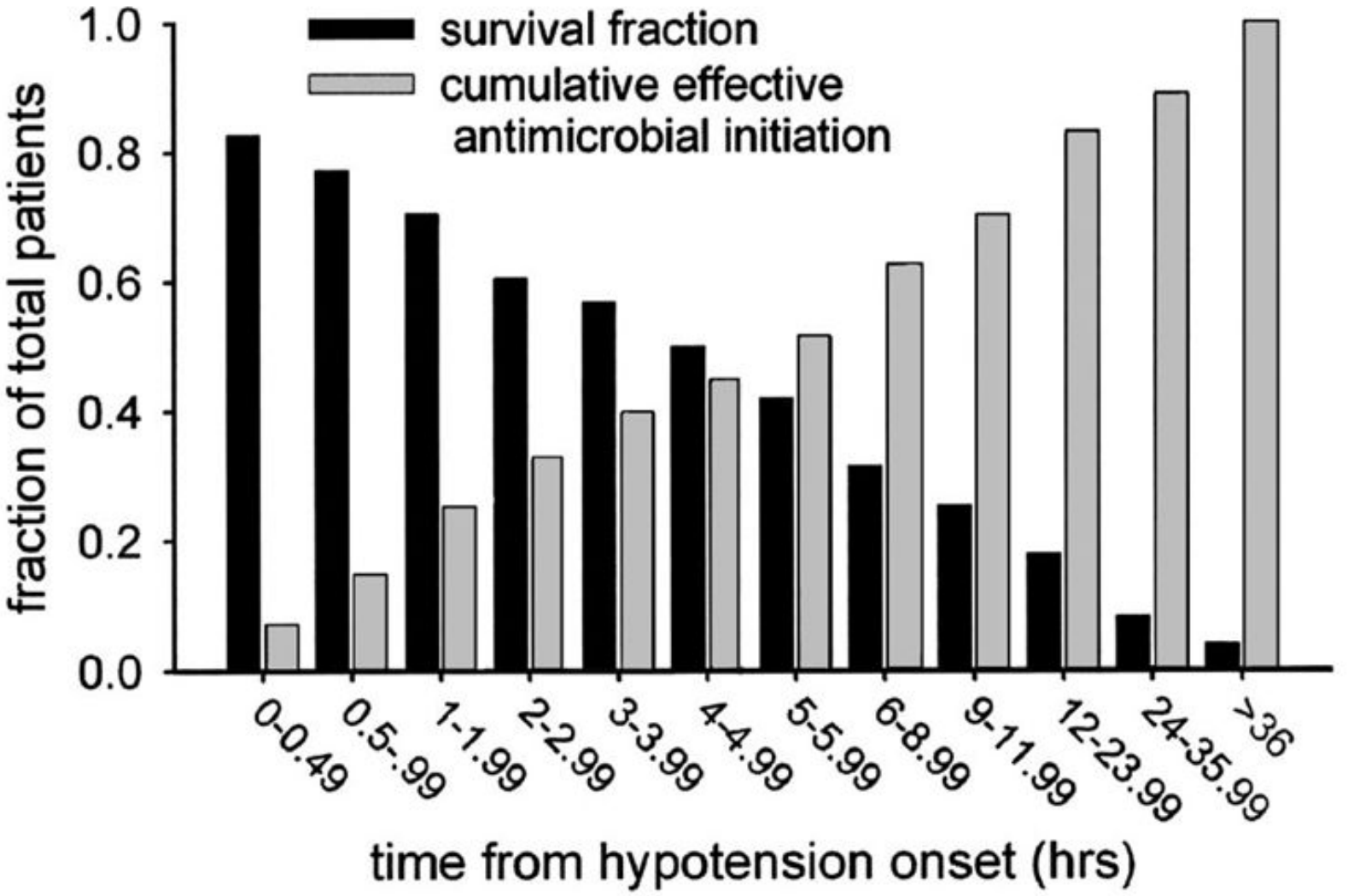
- Efficacy: In RCTS in surgery & trauma it reduces mortality & bleeding by 1/3
- Safety: No increased thromboses after use: indeed may decrease arterial events
- Safety: no neuro events if use 1-2gm
- Other: May reduce post procedure inflammation?



Utako Okamototo with her husband Shosuka discovered tranexamic acid in the 1950 aged 95 with her family

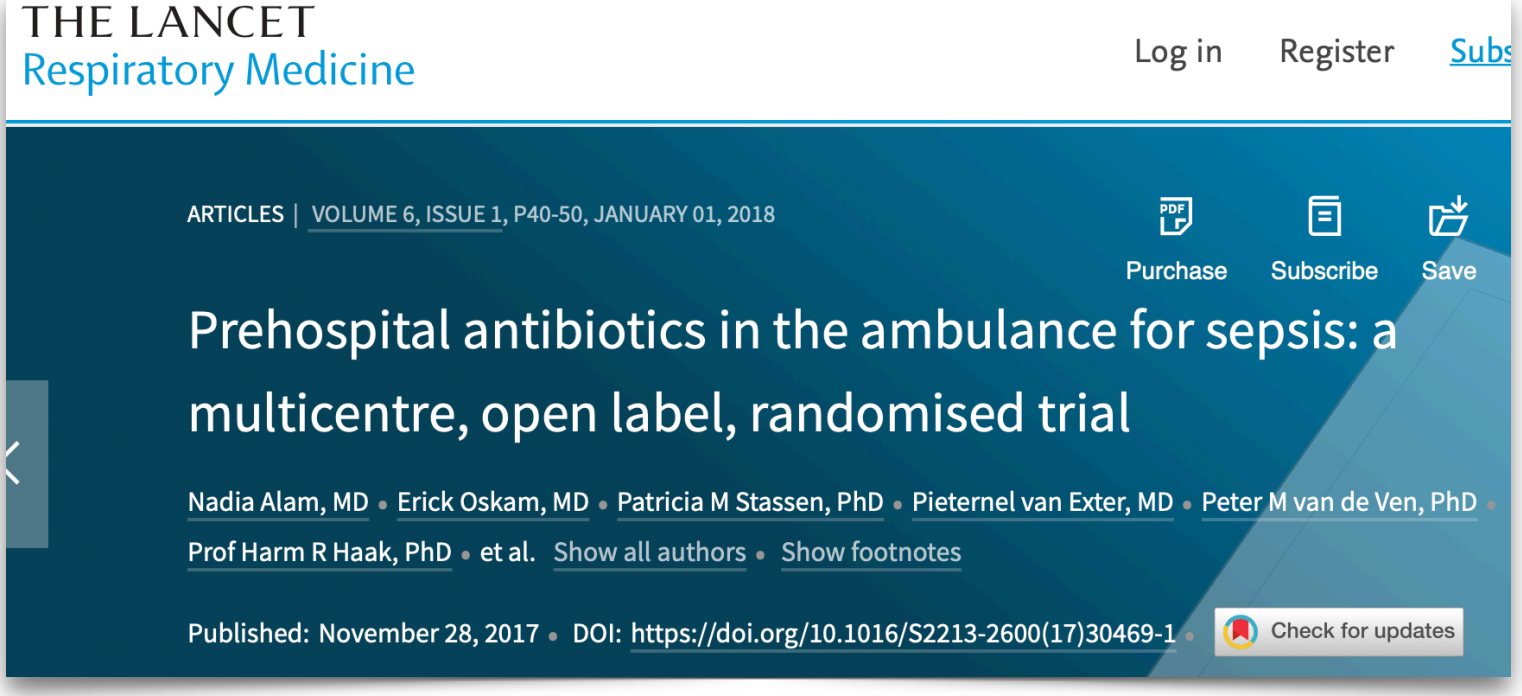

4
ANTIBIOTIKA IM RETTUNGSDIENST?

Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. Kumar et al. Crit Care Med. 2006.

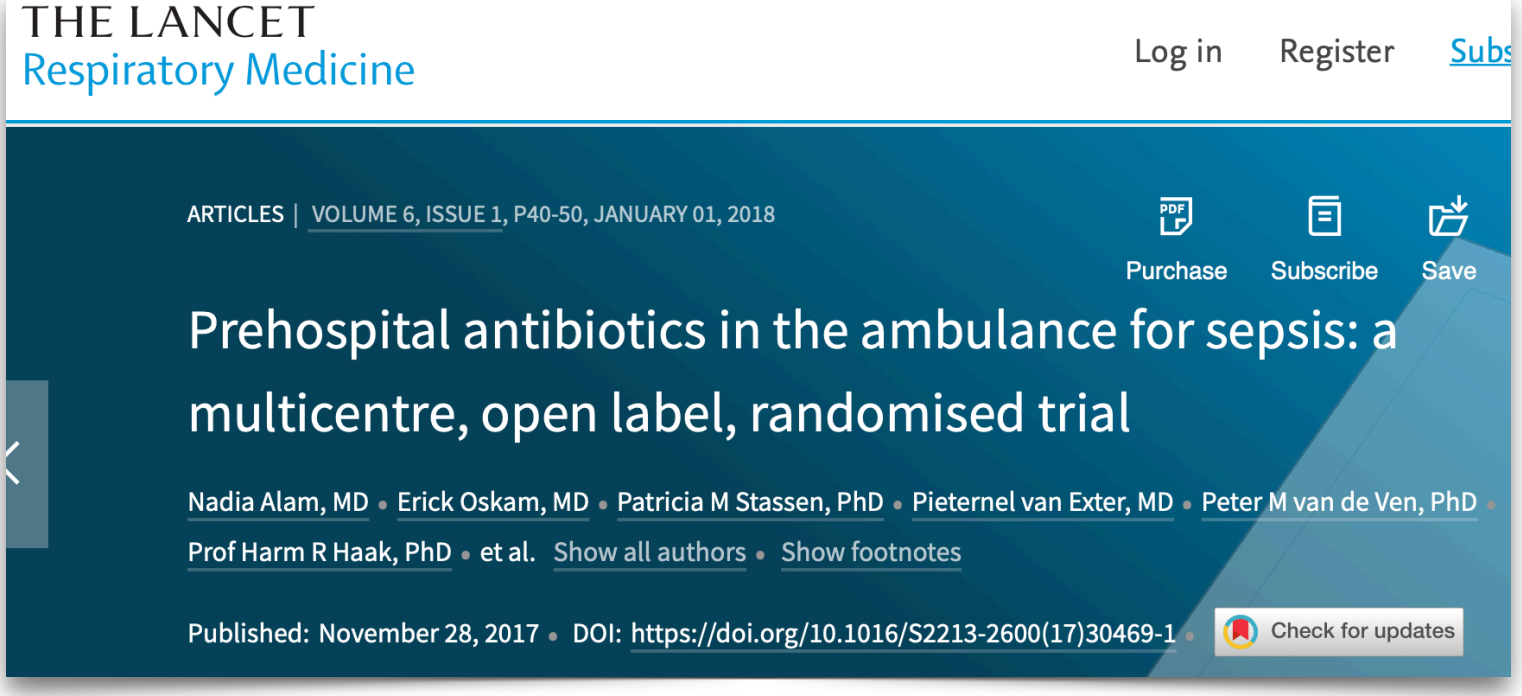


The Question Is…

- Warum also nicht Antibiotika verabreichen, bevor der Patient ins Spital kommt?



- Multicenter, randomisierte Studie
- 2700 Patienten mit Sepsis (def. SIRS, Fieber oder Hypothermie zwingend)
- Vergleich: 2g Rocephin IV vs Standart-Therapie



- Antibiotische Therapie mehr als 90min früher!
- 28-Tage Mortalität kein Unterschied
- Dauer IPS-Aufenthalt oder Spital-Aufenthalt: kein Unterschied

- **‘Pre-Hospital’ Antibiotika im Rettungsdienst sind nutzlos!**

Manage Severe Bleedings like a Pro!

3


Lixiana
Marcoumar
Xarelto
Pradaxa
Eliquis


NDC 63833-387-02
mg
50 mL Single Use Vial

EXPERT CONSENSUS DECISION PATHWAY

2017 ACC Expert Consensus Decision Pathway on Management of Bleeding in Patients on Oral Anticoagulants

A Report of the American College of Cardiology Task Force on Expert Consensus Decision Pathways

Mengenmässig relevante Blutung (Hb-Abfall >20g/L) oder:

TABLE 1 Critical Site Bleeds

Type of Bleed	Initial Signs and Symptoms	Potential Consequences of Bleed
Intracranial hemorrhage: Includes intraparenchymal, subdural, epidural, and subarachnoid hemorrhages	**Unusually intense headache, emesis** **Neurological signs:** e.g., reduced LOC, vision changes, numbness, weakness, aphasia, ataxia, vertigo, seizures	Stupor or coma Permanent neurological deficit Death
Other central nervous system hemorrhage: Includes Intraocular, intra- or extra-axial spinal hemorrhages	**Intraocular:** monocular eye pain, vision changes, blindness **Spinal:** back pain, bilateral extremity weakness or numbness, bowel or bladder dysfunction, respiratory failure	**Intraocular:** permanent vision loss **Spinal:** permanent disability, paraplegia, quadriplegia, death
Pericardial tamponade	Shortness of breath, tachypnea Hypotension, jugular venous distension Tachycardia, muffled heart sounds, rub	Cardiogenic shock Death
Airway, including posterior epistaxis	**Airway:** hemoptysis, shortness of breath, hypoxia **Posterior epistaxis:** profuse epistaxis, hemoptysis, hypoxia, shortness of breath	Hypoxemic respiratory failure, Death
Hemothorax, intra-abdominal bleeding, and RPH	**Hemothorax:** tachypnea, tachycardia, hypotension **Intra-abdominal (nongastrointestinal):** abdominal pain, distension, hypotension, tachycardia **RPH:** Back/flank/hip pain, tachycardia, hypotension	**Hemothorax:** respiratory failure **RPH:** femoral neuropathy **All:** hypovolemic shock, death
Extremity bleeds: includes intramuscular and intra-articular bleeding	**Intramuscular:** pain, swelling, pallor, paresthesia, weakness, diminished pulse **Intra-articular:** joint pain, swelling, decreased range of motion	**Intramuscular:** compartment syndrome, paralysis, limb loss **Intra-articular:** irreversible joint damage

LOC = loss of consciousness; RPH = retroperitoneal hematoma.

EXPERT CONSENSUS DECISION PATHWAY

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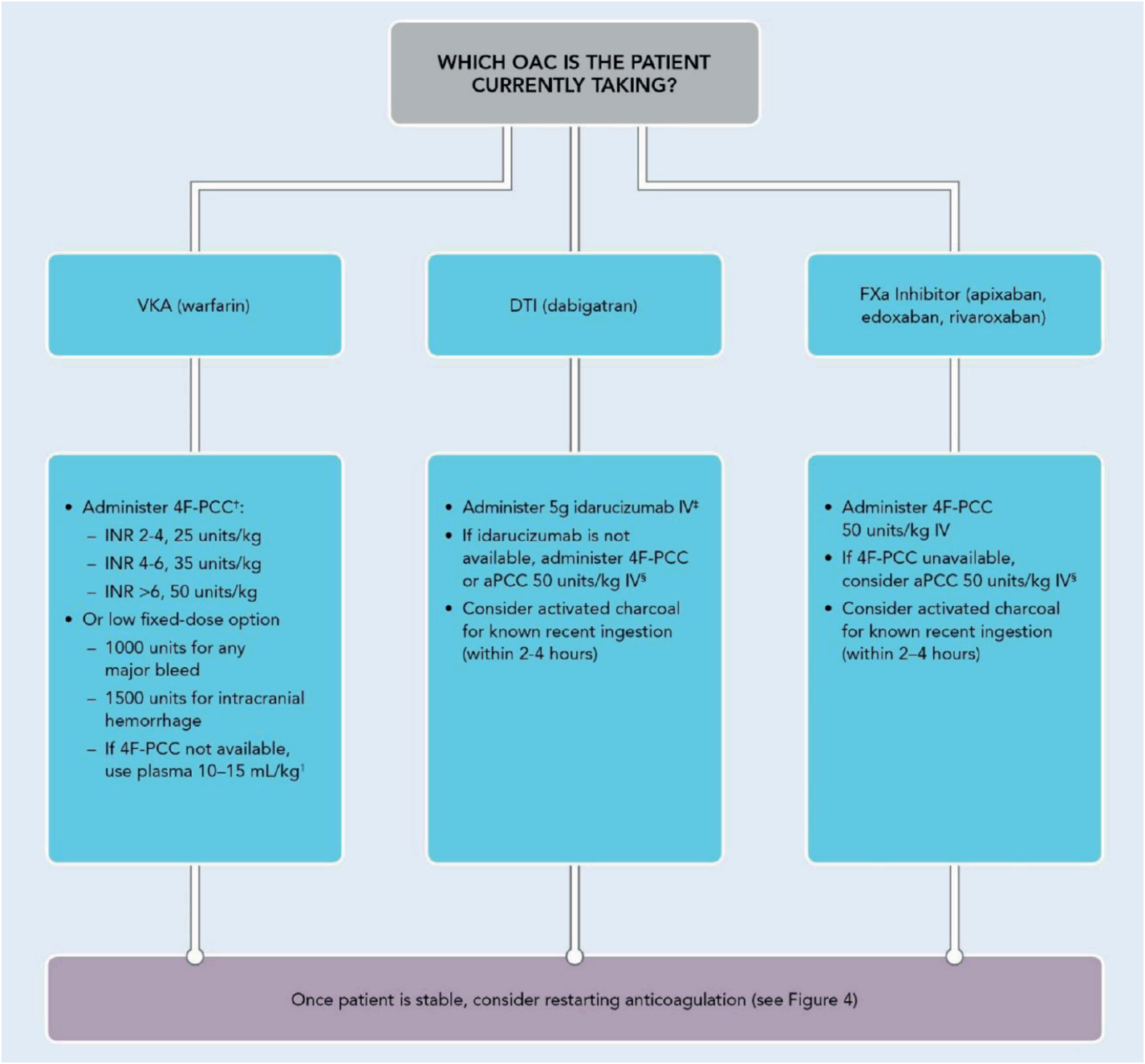
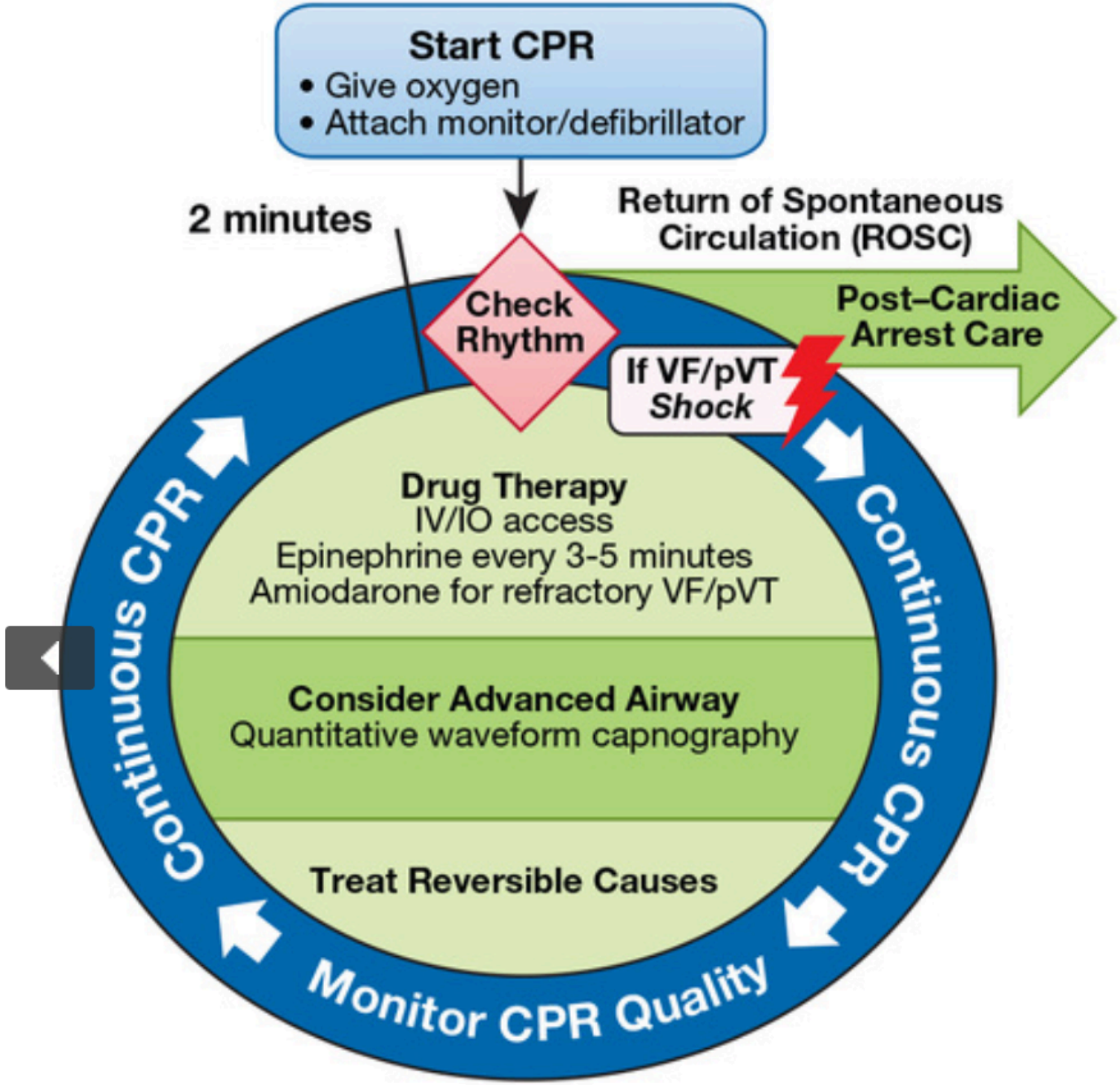
TABLE 3 Suggestions for Laboratory Measurement of DOACs When Specialized Assays are not Available

	Clinical Objective			
	Exclude Clinically Relevant* Drug Levels		Determine Whether On-Therapy or Above On-Therapy Levels Are Present	
Drug	**Suggested Test**	**Interpretation**	**Suggested Test**	**Interpretation**
Dabigatran	TT, aPTT	**Normal TT** excludes clinically relevant* levels **Prolonged TT** does not discriminate between clinically important and insignificant levels **Normal aPTT** usually excludes clinically relevant* levels, if a sensitive reagent is used.	aPTT	**Prolonged aPTT** suggests that on-therapy or above on-therapy levels are present **Normal aPTT** may not exclude on-therapy levels, particularly if a relatively insensitive aPTT reagent is used
Apixaban	None	**Normal PT and aPTT** do not exclude clinically relevant* levels	PT	**Prolonged PT** suggests that on-therapy or above on-therapy levels are present **Normal PT** may not exclude on-therapy *or above on-therapy levels*, particularly if a relatively insensitive PT reagent is used
Edoxaban or rivaroxaban	None	**Normal PT and aPTT** do not exclude clinically relevant* levels	PT	**Prolonged PT** suggests that on-therapy or above on-therapy levels are present **Normal PT** may not exclude on-therapy levels, particularly if a relatively insensitive PT reagent is used


WHICH OAC IS THE PATIENT CURRENTLY TAKING?
VKA (warfarin)
DTI (dabigatran)
FXa Inhibitor (apixaban, edoxaban, rivaroxaban)
• Administer 4F-PCC†:
– INR 2-4, 25 units/kg
– INR 4-6, 35 units/kg
– INR >6, 50 units/kg
• Or low fixed-dose option
– 1000 units for any major bleed
– 1500 units for intracranial hemorrhage
– If 4F-PCC not available, use plasma 10–15 mL/kg‡
• Administer 5g idarucizumab IV‡
• If idarucizumab is not available, administer 4F-PCC or aPCC 50 units/kg IV§
• Consider activated charcoal for known recent ingestion (within 2-4 hours)
• Administer 4F-PCC 50 units/kg IV
• If 4F-PCC unavailable, consider aPCC 50 units/kg IV§
• Consider activated charcoal for known recent ingestion (within 2–4 hours)
Once patient is stable, consider restarting anticoagulation (see Figure 4)

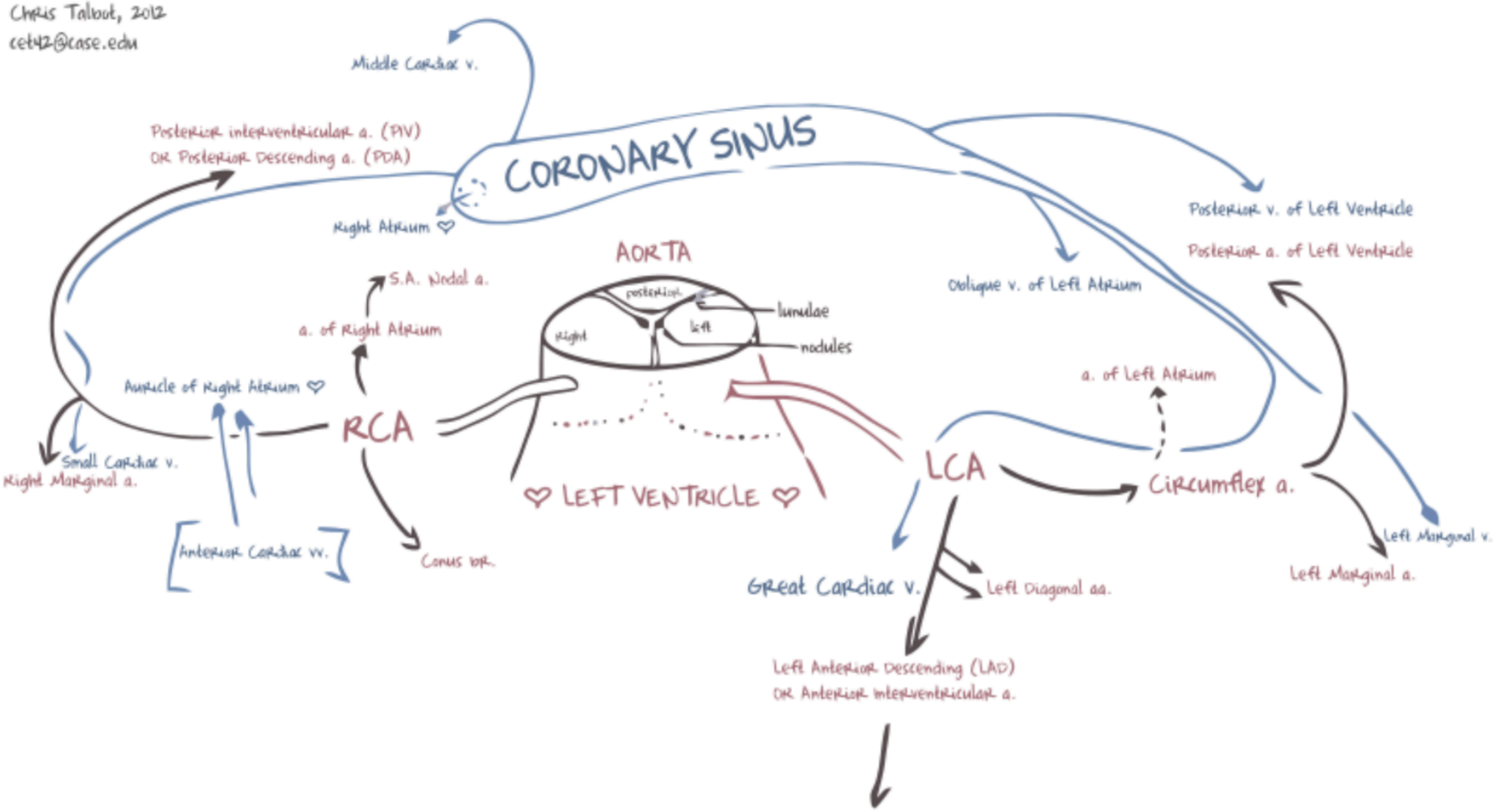

2
Kein Adrenalin?
Kein Problem!


Start CPR
• Give oxygen
• Attach monitor/defibrillator
2 minutes
Check Rhythm
Return of Spontaneous Circulation (ROSC)
Post–Cardiac Arrest Care
If VF/pVT
Shock
Drug Therapy
IV/IO access
Epinephrine every 3-5 minutes
Amiodarone for refractory VF/pVT
Consider Advanced Airway
Quantitative waveform capnography
Treat Reversible Causes
Continuous CPR
Continuous CPR
Monitor CPR Quality

Adrenalin, Epinephrine, Suprarenin

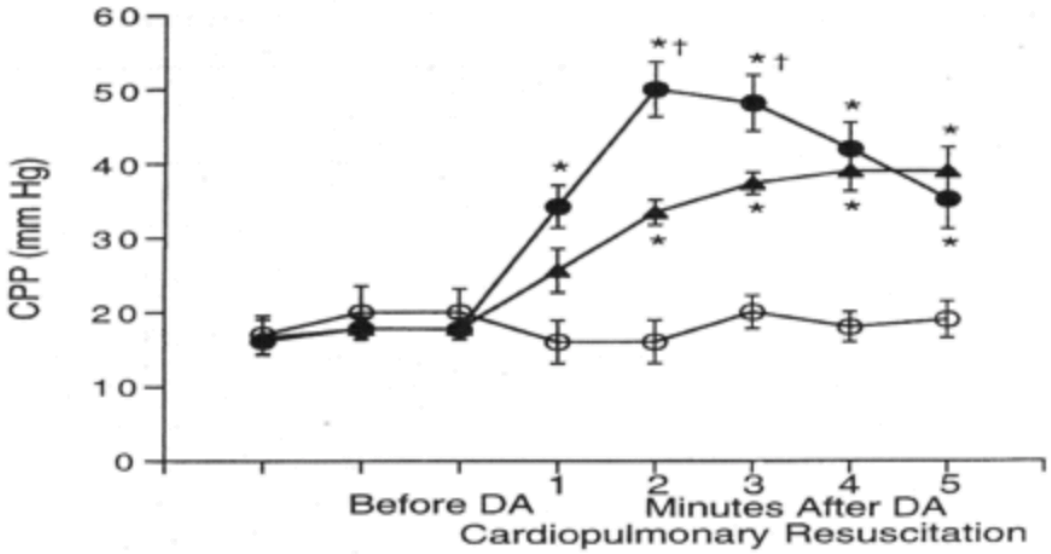
- Das MUSS bei einer Reanimation!
- Eine REA ohne: Unvorstellbar!

Chris Talbot, 2012
ctt42@case.edu



Coronary Perfusion Pressure CPP

Fig. 6



View large Download slide

Coronary perfusion pressure before and after endobronchial drug administration during CPR. All variables are given as mean±S.E.M.; DA, drug administration; CPP, coronary perfusion pressure; intravenous vasopressin (●); endobronchial vasopressin (▲); endobronchial saline placebo (○); *, $P<0.05$ compared with endobronchial saline placebo; †, $P<0.05$

- „Bisher existierte keine placebo-kontrollierte Studie, die belegen konnte, dass der routinemäßige Gebrauch eines Vasopressors in irgendeinem Stadium des menschlichen Kreislaufstillstands das Patientenüberleben mit guter neurologischer Erholung bei der Klinikentlassung verbessert.”

The Question Is…

- Verbessert die Verabreichung von Epinephrin im Vergleich zu Placebo bei erwachsenen Patienten mit außerklinischem Herzstillstand (OOHCA) das Überleben?

ORIGINAL ARTICLE FREE PREVIEW

A Randomized Trial of Epinephrine in Out-of-Hospital Cardiac Arrest

Gavin D. Perkins, M.D., Chen Ji, Ph.D., Charles D. Deakin, M.D., Tom Quinn, M.Phil., Jerry P. Nolan, M.B., Ch.B., Charlotte Scomparin, M.Sc., Scott Regan, B.A., John Long, Anne Slowther, Ph.D., Helen Pocock, M.Sc., John J.M. Black, M.B., B.S., Fionna Moore, M.B., B.S., et al., for the PARAMEDIC2 Collaborators*

- ILCOR initiiert, NHS Ambulance Service
- Randomisierte Doppel-Blind-Studie
- 1mg Adrenalin vs NaCl 0.9%
- >16 Jahre mit OOHCA, ACLS Guidelines
  - Nur 21% der Patienten hatten einen initial schockierteren Rhythmus
- insgesamt 8014 Patienten included

ORIGINAL ARTICLE FREE PREVIEW

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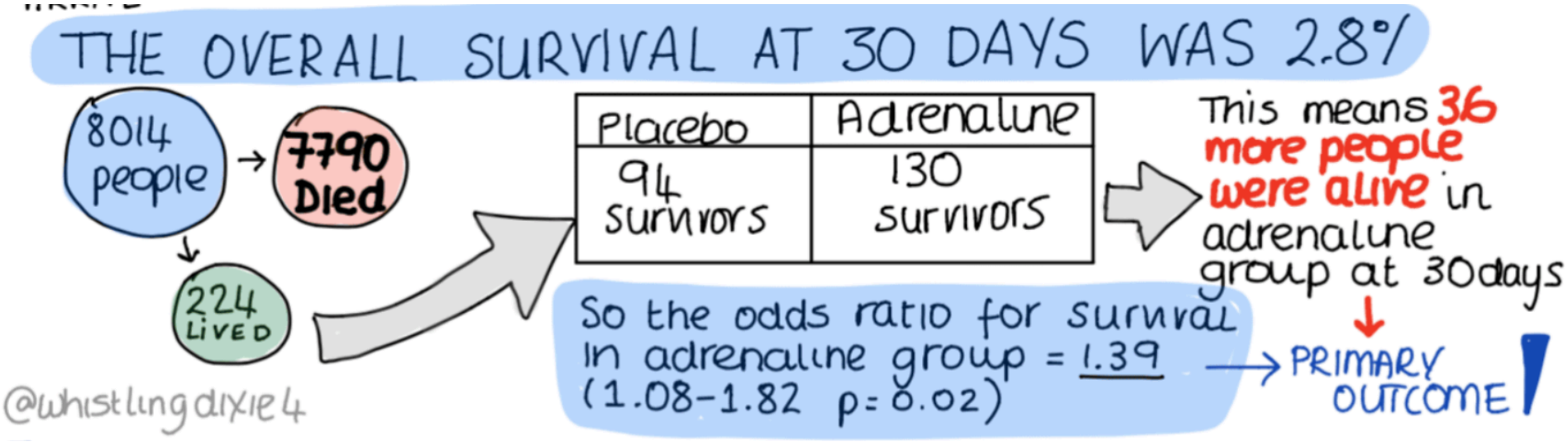

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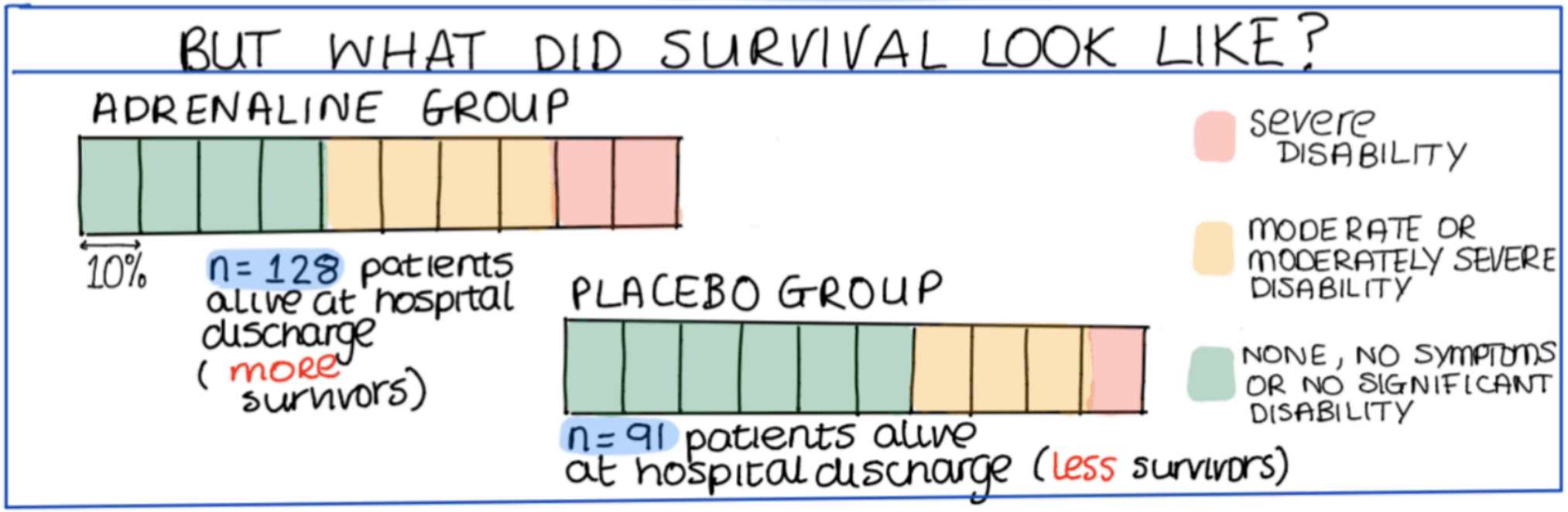
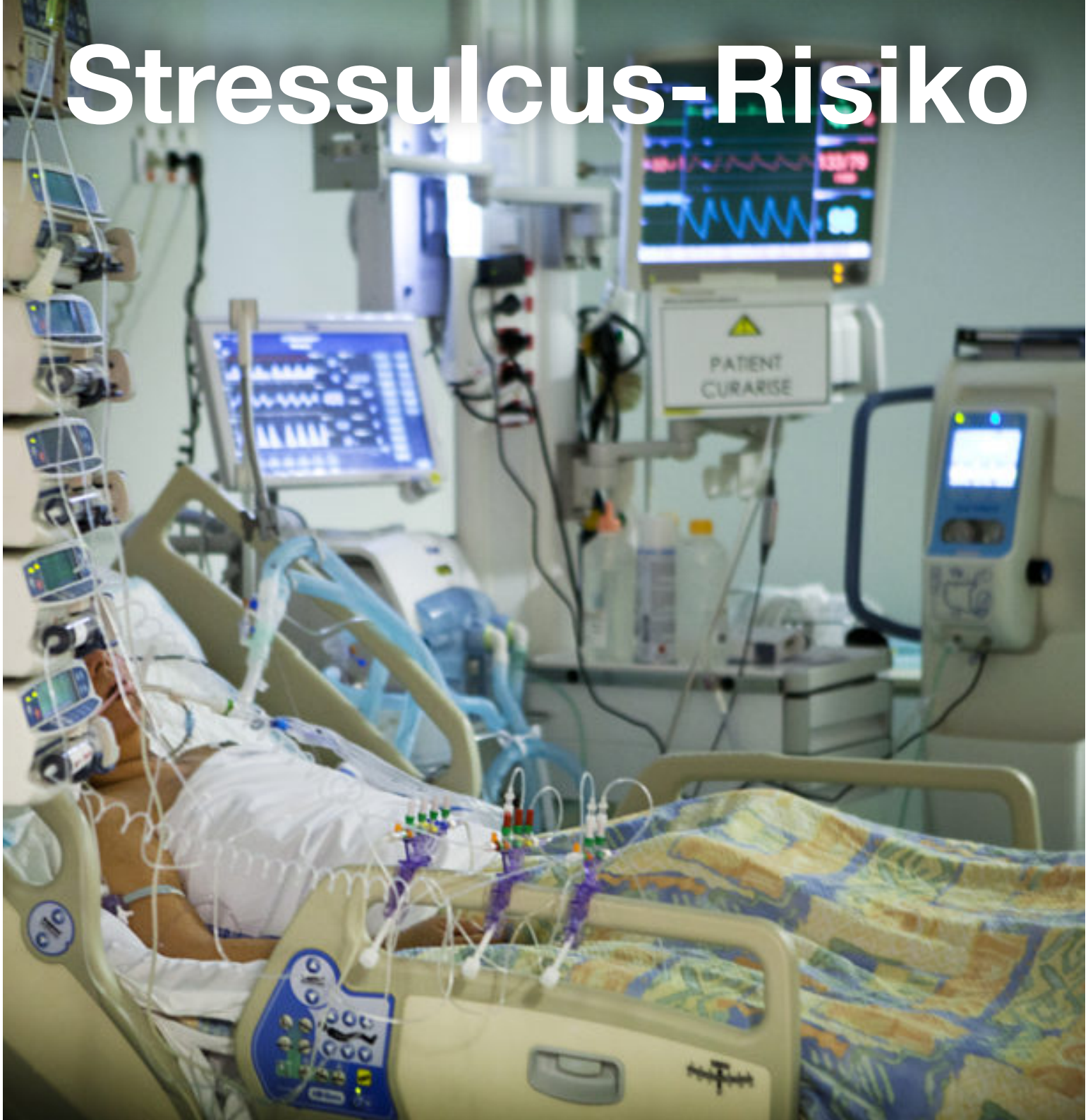


- **Paramedic 2 suggeriert, dass Adrenalin bei der Reanimation die 30-Tage Mortalität verringert…**
- **… dies aber auf Kosten eines schlechteren neurologischen Outcomes!**
- **Einmal mehr wird klar: Es muss mehr gemacht werden, um eine frühzeitige CPR und die Verfügbarkeit von AED's sicherzustellen!**


Do You Still
SUP?
1

Stressulcus-Risiko



Schock

Invasiv-mechanische Beatmung

Nierenersatzverfahren

Koagulopatie

Antikoagulation

Traumatische Hirnschädigung


PANTOZOL
PANTOPRAZOL
Tabletas
40 mg
Caja con 14 tabletas
Dead heart muscle

The Question Is…

- Reduziert der Einsatz von prophylaktischem Protonenpumpenhemmer (PPI) im Vergleich zu Placebo bei Patienten auf der Intensivstation, die von gastrointestinalen (GI) Blutungen bedroht sind, die Sterblichkeit nach 90 Tagen?

SUP-ICU

- Multicenter, randomisierte, placebo-kontrollierte, verblindete Studie
- 33 Intensivstationen in 6 europäischen Ländern (u.a. der Schweiz)
- 3298 Patienten rekrutiert
- Pantoprazole 40mg IV OD vs NaCl 0.9%
  - Bis Entlassung IPS oder versterben

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Pantoprazole in Patients at Risk for Gastrointestinal Bleeding in the ICU

SUP-ICU

Primary Outcome				
Measure	**Pantoprazole**	**Control**	**ARR/I**	**NNT/H**
90 day all-cause mortality (%)	31.1	30.4	ARI 0.63 (CI -2.52 to 3.79, p=0.7)	NNH 159
ARR/I = absolute risk reduction; CI = confidence interval; p = p-value; NNT/H = number needed to treat/harm				

Secondary Outcomes				
Measure	**Pantoprazole**	**Control**	**ARR/I**	**NNT/H**
1 or more clinically important events (%)	21.9	22.6	ARR 0.7 (CI -2.13 to 3.56, p=0.6)	NNT 140
1 or more clinically important GI bleeds (%)	2.5	4.2	ARR 1.7 (CI 0.47 to 2.92, p=0.009)	NNT 59
1 or more infectious adverse events (%)	16.8	16.9	ARR 0.05 (CI -2.5 to 2.6, p=1.0)	NNT 2027
Severe adverse reactions	0	0		
Median % of days alive without use of life support	92	92		
ARR/I = absolute risk reduction; CI = confidence interval; p = p-value; NNT/H = number needed to treat/harm				

- **PPI's bringen bei IPS-Patienten mit GI-Blutungsrisiko keinen Mortalitäts-Benefit**

- **Die Inzidenz von klinisch relevanten GI-Blutungen ist unter PPI's tiefer**

Aber: PPI's bei Möglichkeit wieder stoppen (enterale Ernährung)!


#1


Thanks for watching!
https://www.crit.cloud/download-presentations.html