

VMC Grand Rounds Pulmonary/Critical Care Updates 2022



Richard Kim, MD
Valley Medical Center



Relevant Disclosures

- None



You're on call



Taken from Houston Chronicle website



WE ARE *Valley*



Hour 1: You get a call to the ED

- 64M, found unresponsive by family, unknown down time, initial rhythm V.fib, achieved ROSC after several rounds of CPR, intubated in field.
- EKG, CTPA, CT head, tox screen unremarkable
- Stable, aside from norepinephrine gtt
- “Should we cool him?”



History of Targeted Temperature Management

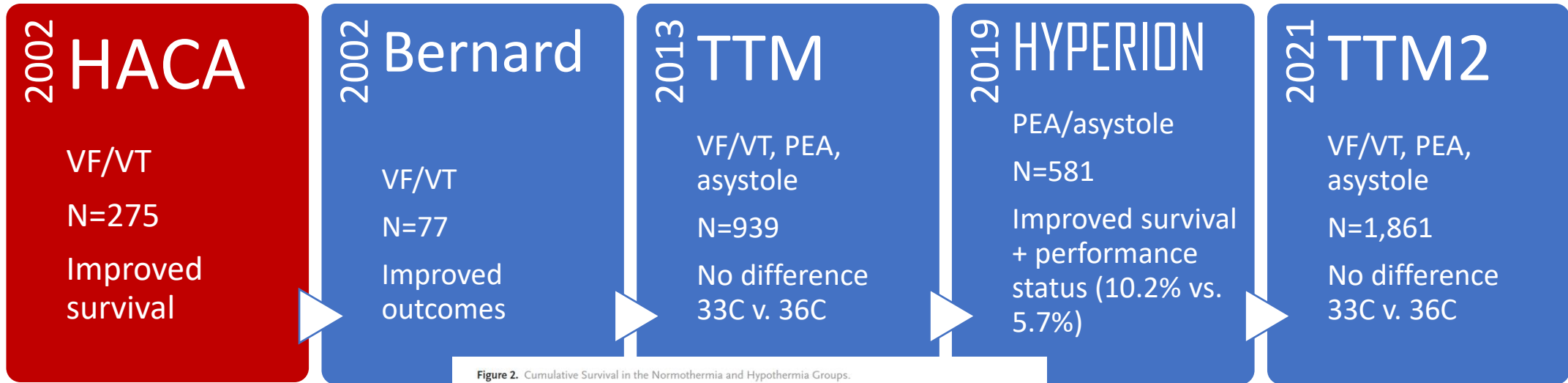
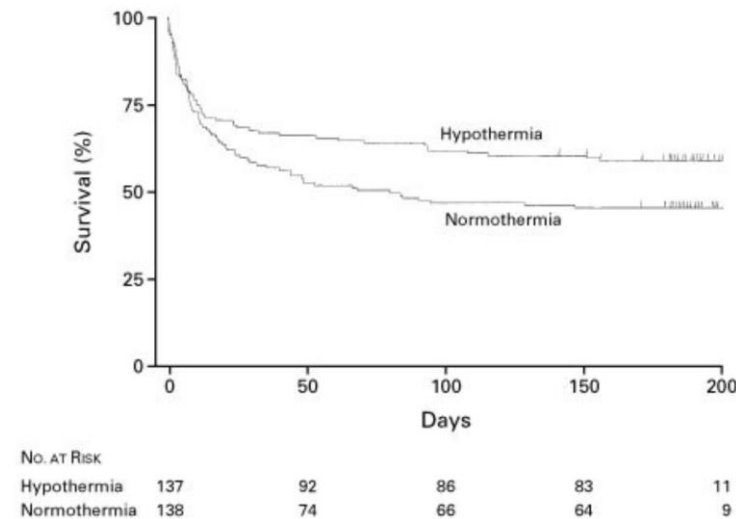


Figure 2. Cumulative Survival in the Normothermia and Hypothermia Groups.



Censored data are indicated by tick marks.

History of Targeted Temperature Management

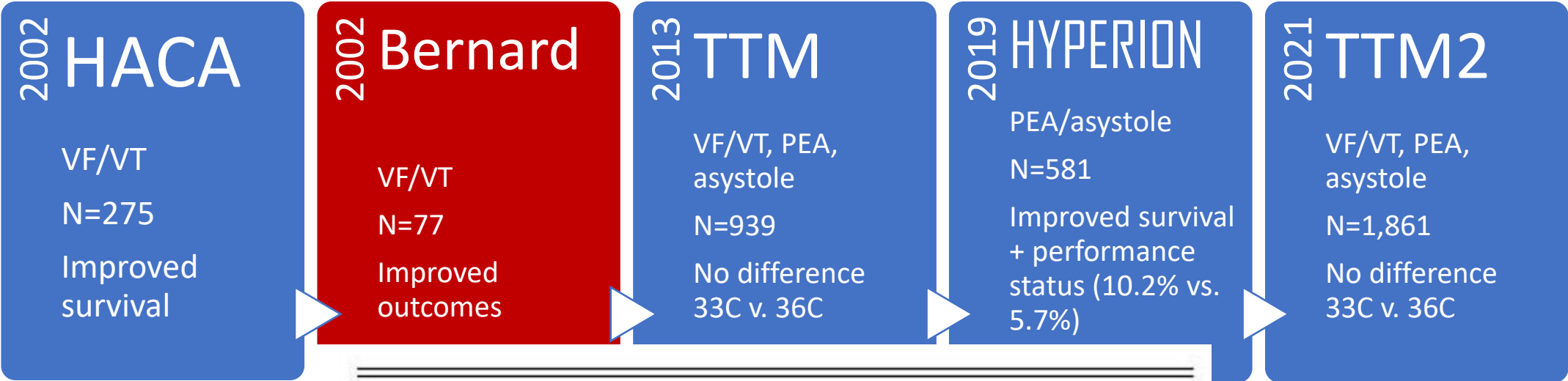
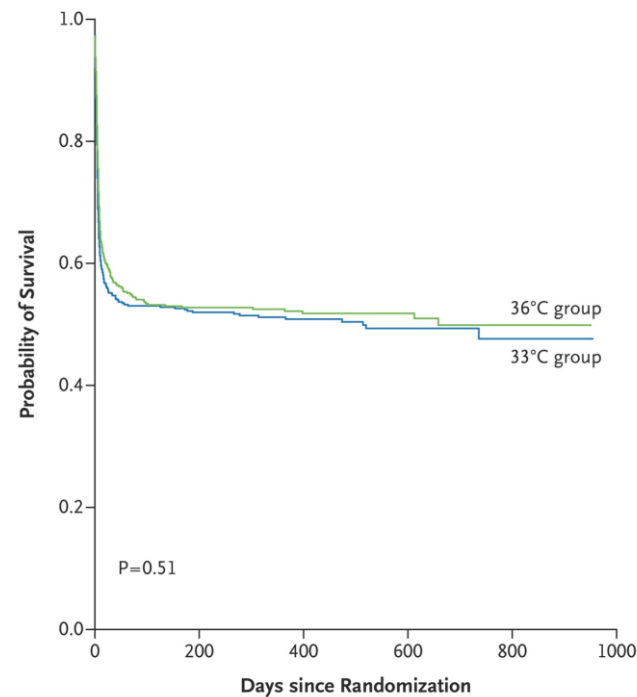
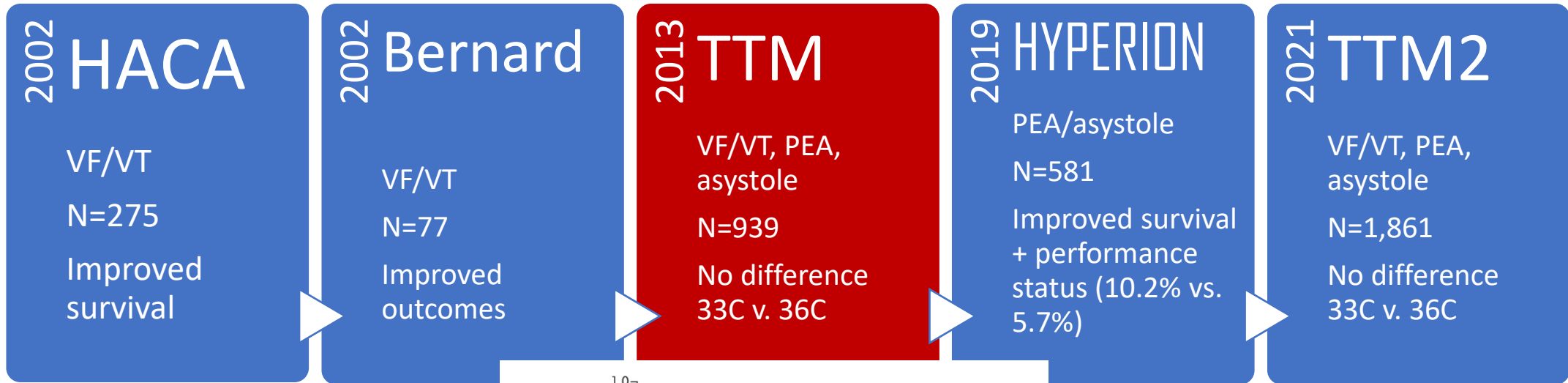


TABLE 5. OUTCOME OF PATIENTS AT DISCHARGE FROM THE HOSPITAL.

OUTCOME*	HYPOTHERMIA (N = 43)	NORMOTHERMIA (N = 34)
	number of patients	
Normal or minimal disability (able to care for self, discharged directly to home)	15	7
Moderate disability (discharged to a rehabilitation facility)	6	2
Severe disability, awake but completely	0	1

History of Targeted Temperature Management



History of Targeted Temperature Management

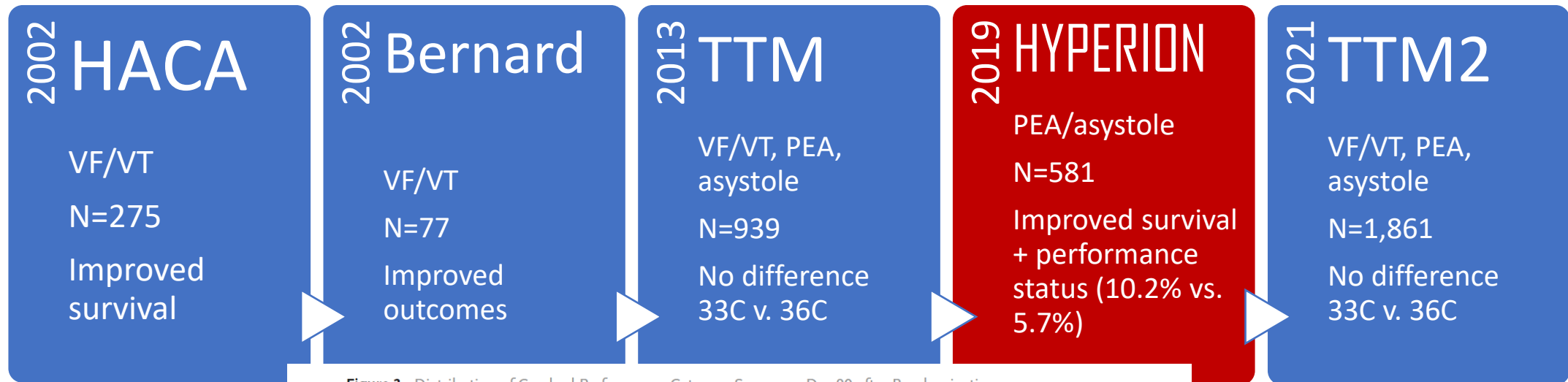
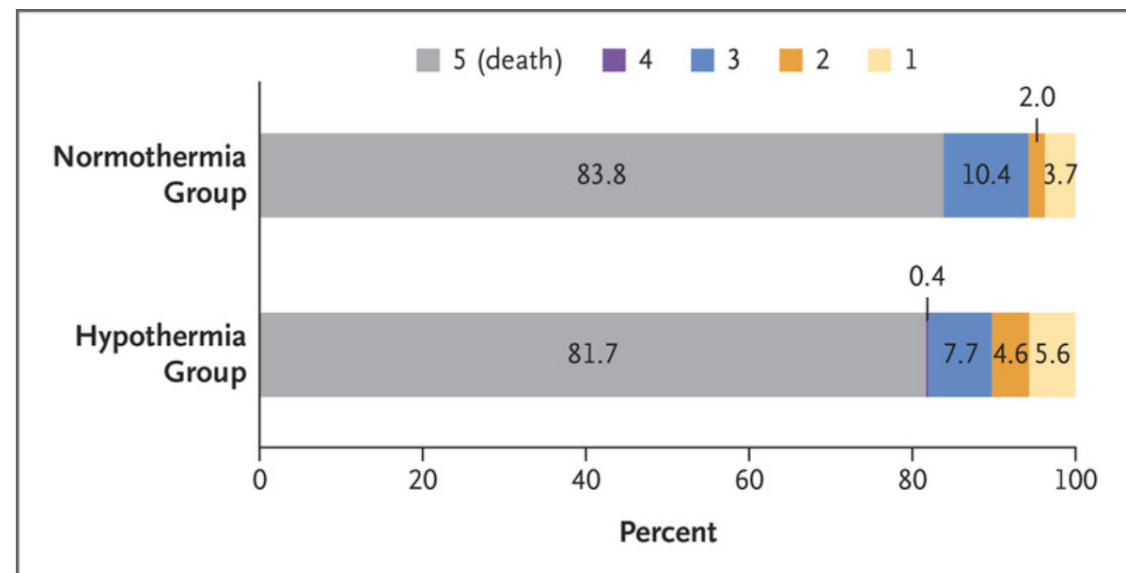


Figure 3. Distribution of Cerebral Performance Category Scores on Day 90 after Randomization.



History of Targeted Temperature Management

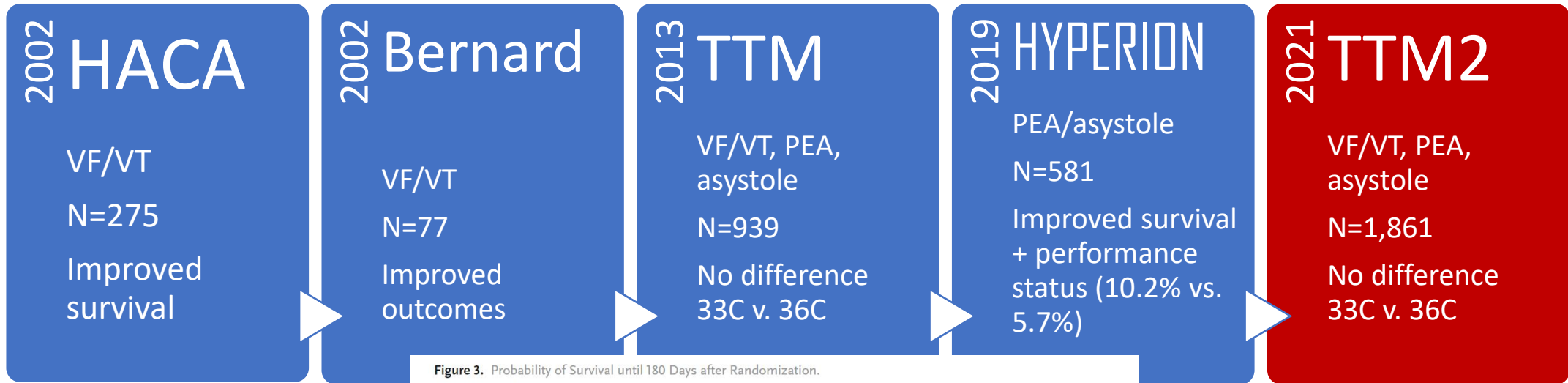
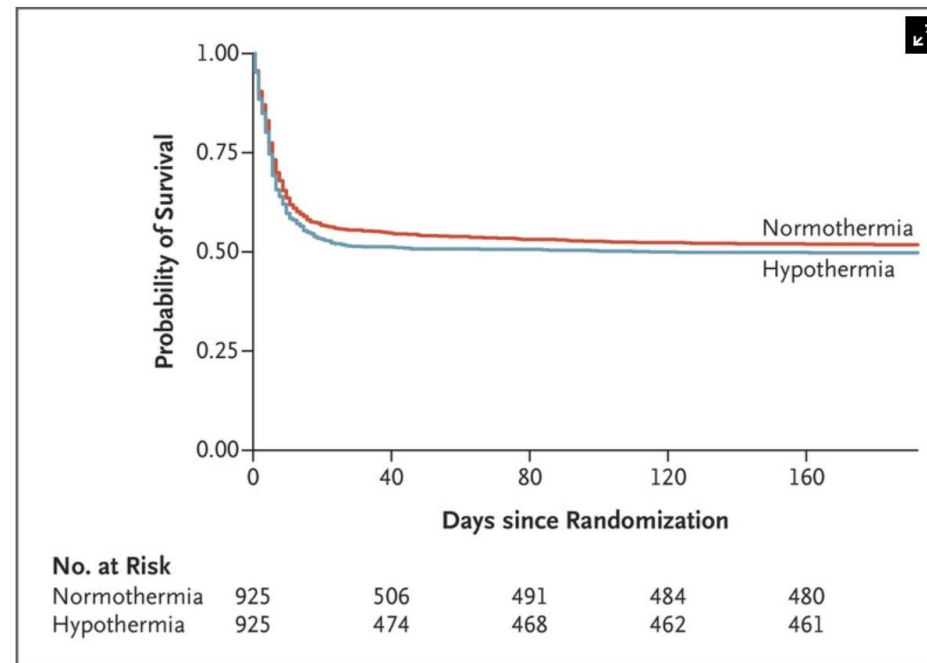
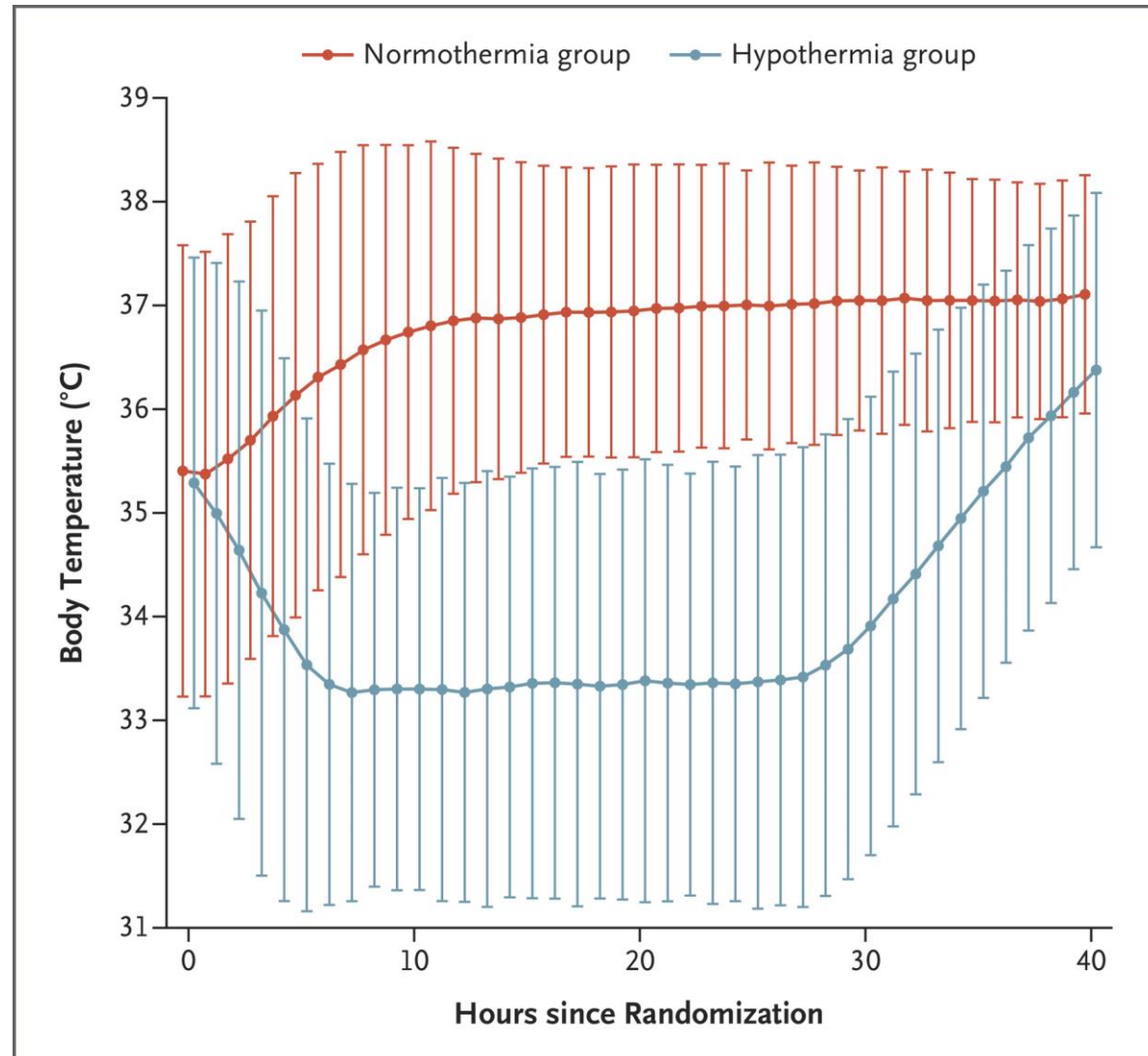


Figure 3. Probability of Survival until 180 Days after Randomization.

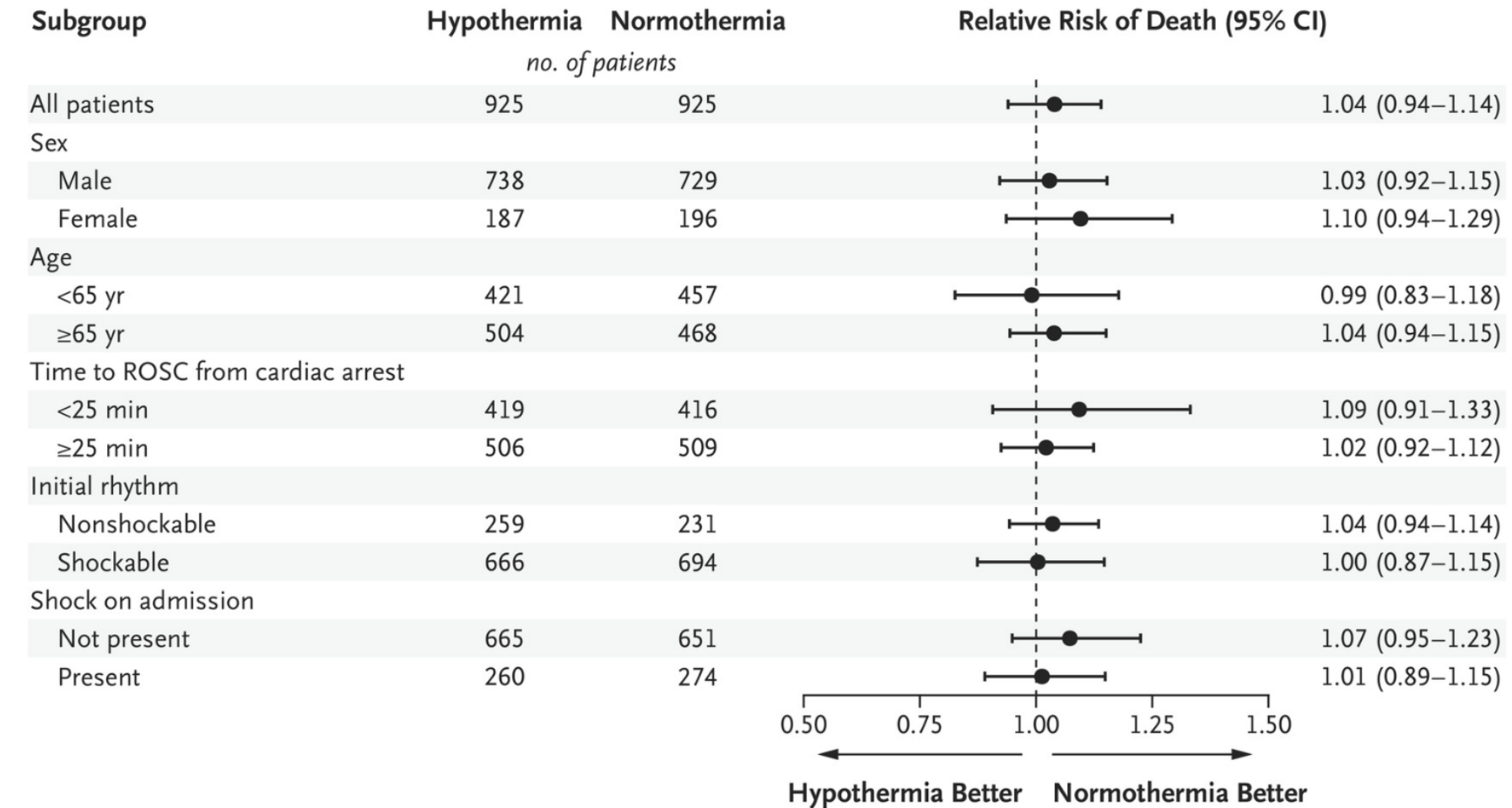


TTM2



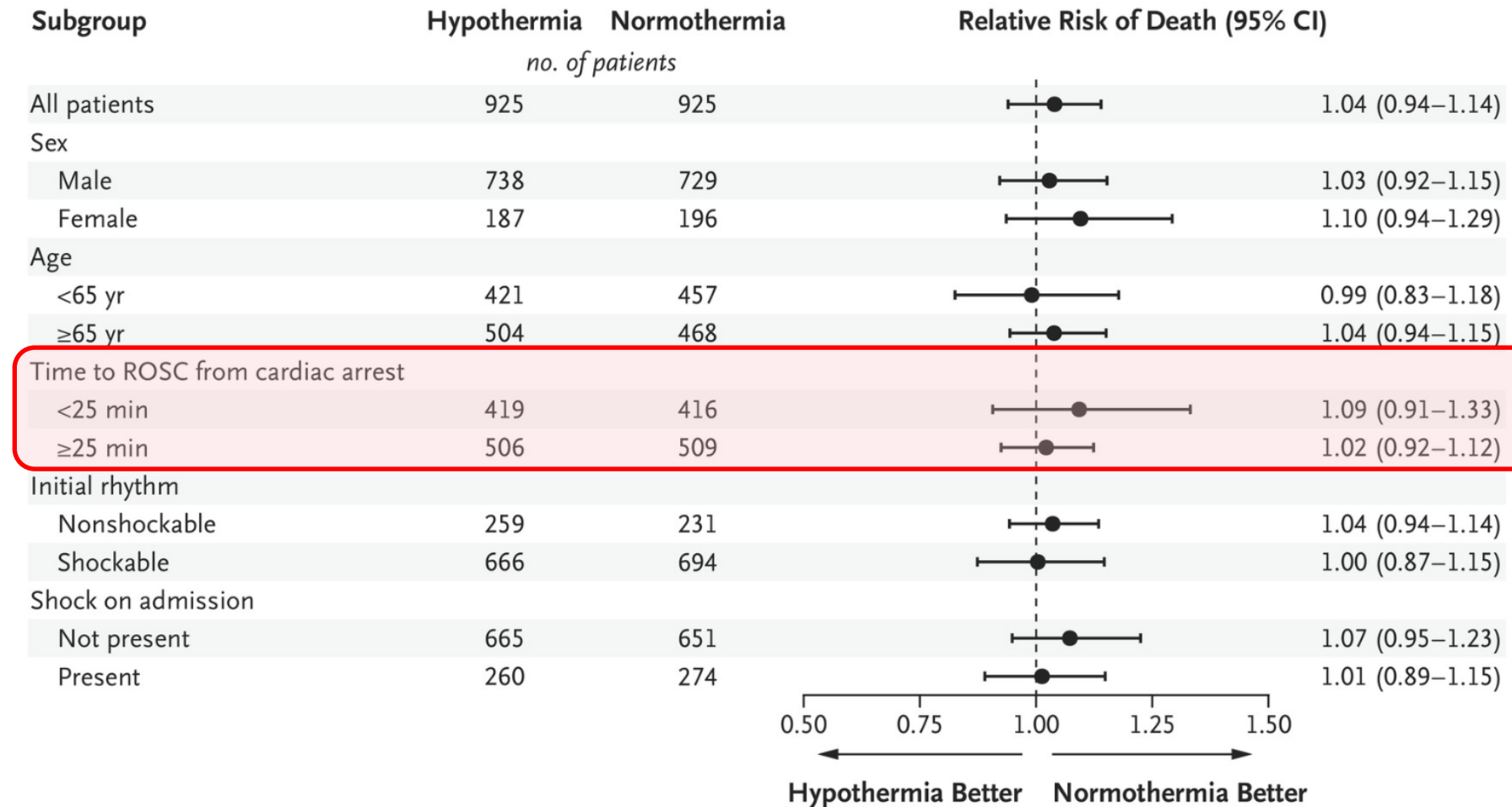
TTM2

A Death at 6 Months



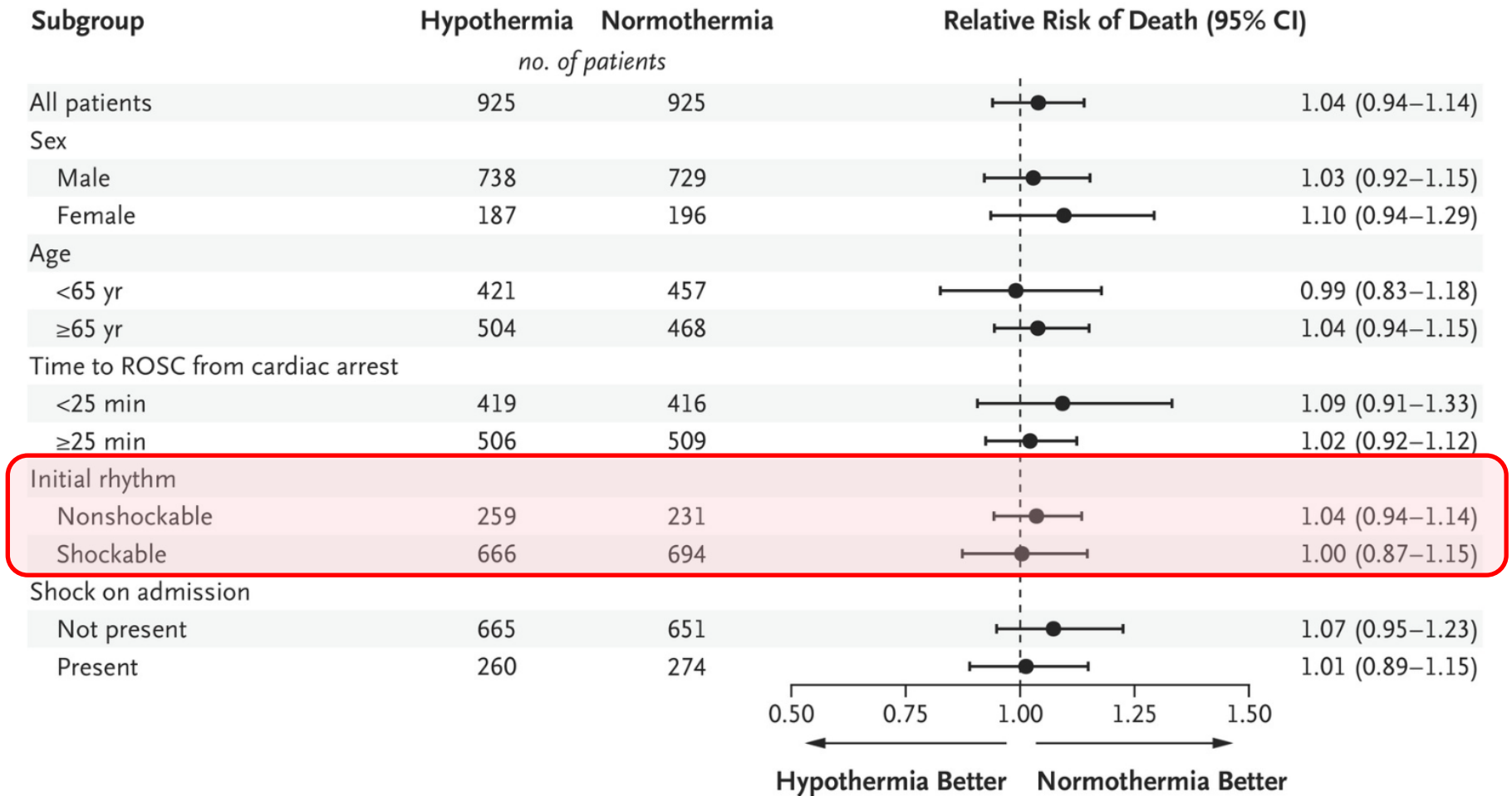
TTM2

A Death at 6 Months



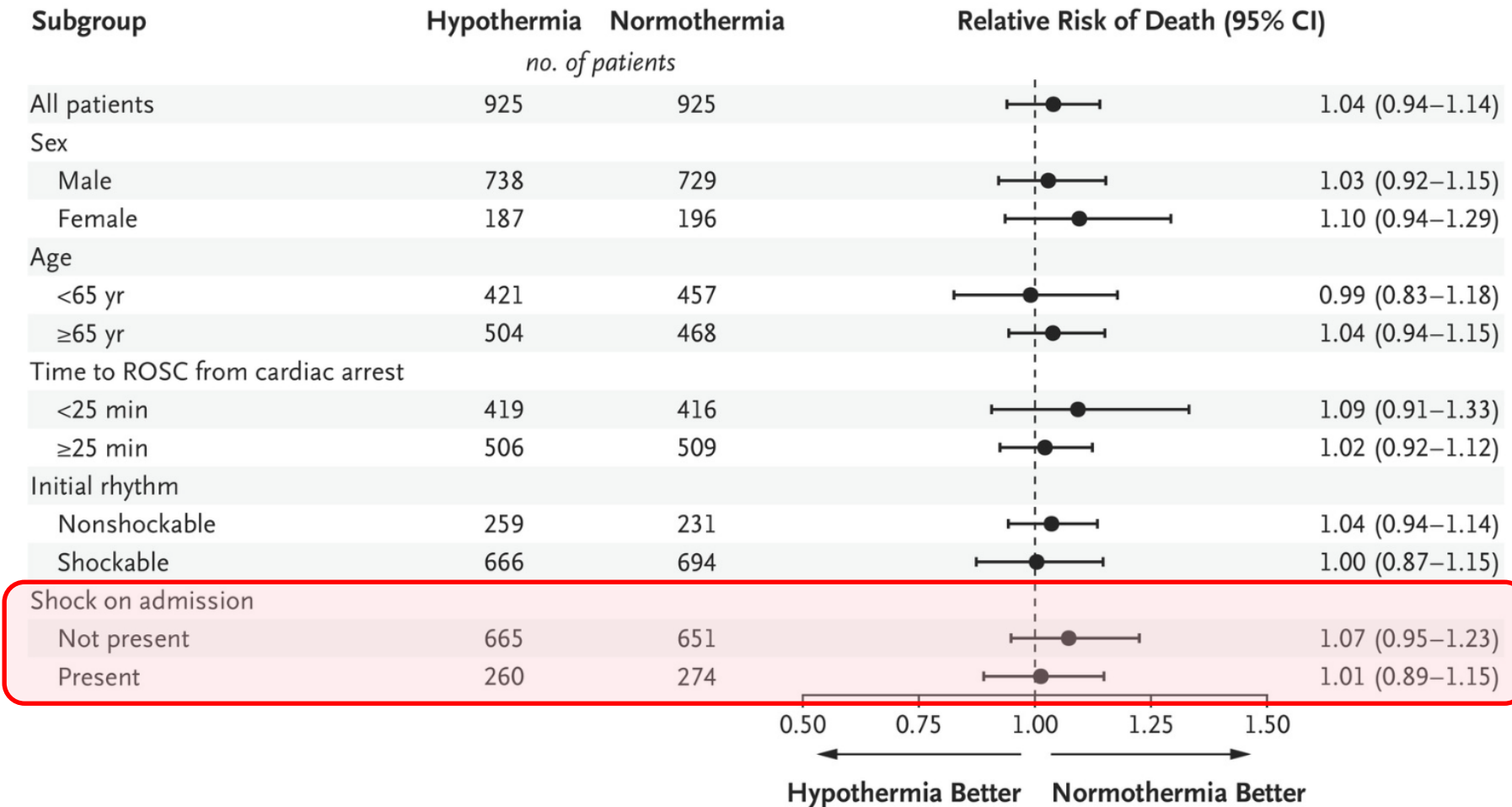
TTM2

A Death at 6 Months

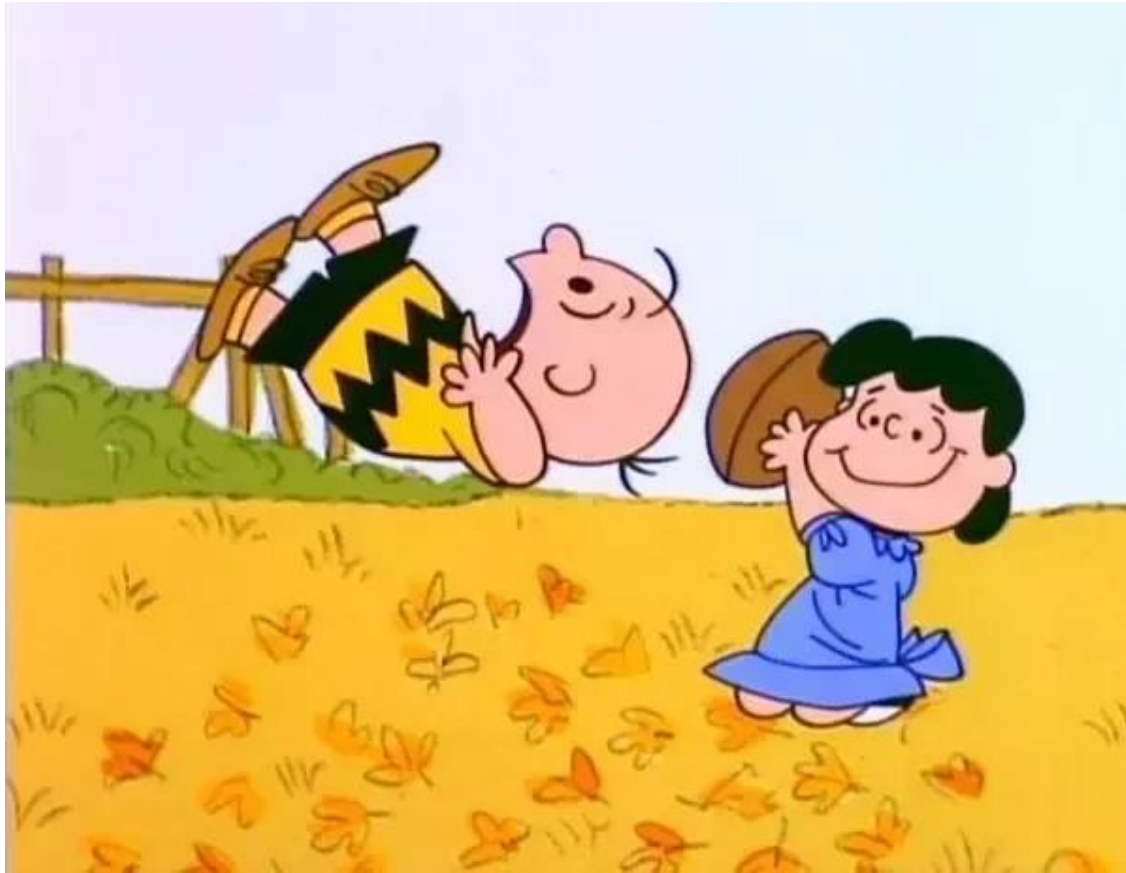


TTM2

A Death at 6 Months



Going forward



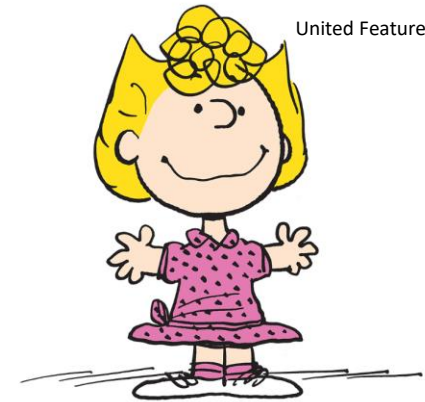
United Feature Syndicate



"Nothing ever works.
Don't cool him."



"Have you considered the potential complications of cooling? We could be doing more harm than good! Let's not cool him."



United Feature Syndicate

"I know he'll wake up. Let's give him the best chance and cool him."



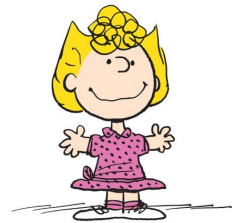
"It's still our policy to cool these patients. Come back here and insert the cooling catheter, you blockhead!"

Table 2. Outcomes and Adverse Events.

Outcome or Event	Hypothermia (N=930)	Normothermia (N=931)	Relative Risk (95% CI)*	P Value
Primary outcome: death from any cause at 6 mo — no./total no. (%)	465/925 (50)	446/925 (48)	1.04 (0.94–1.14)	0.37
Main secondary outcome — no./total no. (%)				
Score of 4–6 on modified Rankin scale at 6-mo follow-up†	488/881 (55)	479/866 (55)	1.00 (0.92–1.09)	
Poor functional outcome at 6 mo‡	495/918 (54)	493/911 (54)	1.00 (0.91–1.08)	
Score on modified Rankin scale at 6-mo follow-up — no./total no. (%)†				
0	140/881 (16)	148/866 (17)		
1	87/881 (10)	80/866 (9)		
2	132/881 (15)	127/866 (15)		
3	34/881 (4)	32/866 (4)		
4	16/881 (2)	20/866 (2)		
5	7/881 (1)	13/866 (2)		
6	465/881 (53)	446/866 (52)		
Serious adverse events — no./total no. (%)				
Arrhythmia resulting in hemodynamic com- promise	222/927 (24)	152/921 (16)	1.45 (1.21–1.75)	<0.001
Bleeding	44/927 (5)	46/922 (5)	0.95 (0.63–1.42)	0.81
Skin complication related to device used for targeted temperature management	10/927 (1)	5/922 (<1)	1.99 (0.71–6.37)	0.21
Pneumonia	330/927 (36)	322/921 (35)	1.02 (0.90–1.15)	0.75
Sepsis	99/926 (11)	83/922 (9)	1.19 (0.90–1.57)	0.23

What shall we do?

- The Default position: Let's start cooling him, but abandon if:
 - Any clinical instability, including significant pressor requirements
 - Resource limitations
- The counterargument to continue cooling:
 - HYPERION (survival 18%) fits our population better than TTM2 (survival 51%)
 - Awaiting ICECAP results
 - ICECAP: Influence of Cooling Duration on Efficacy in Cardiac Arrest Patients
 - Cool withing 4 hours, duration 6-72 hours

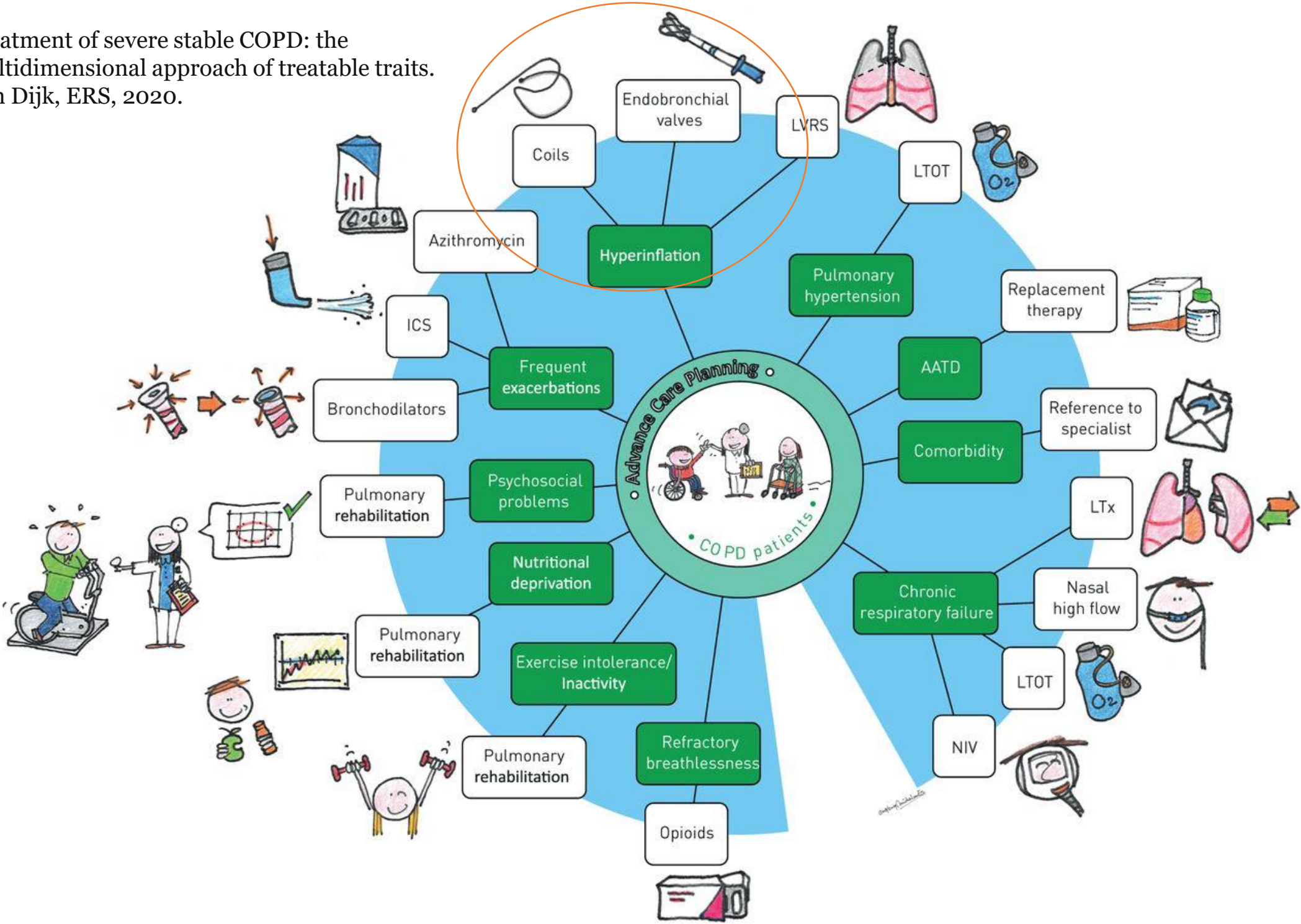


Hour 3: You check on a COPD “frequent flyer”

- 76 M, Stage 4 COPD, admitted two days ago, doing better. You say hi, and he asks about your opinion on endobronchial valves.
- “What’s new with COPD therapeutics?”



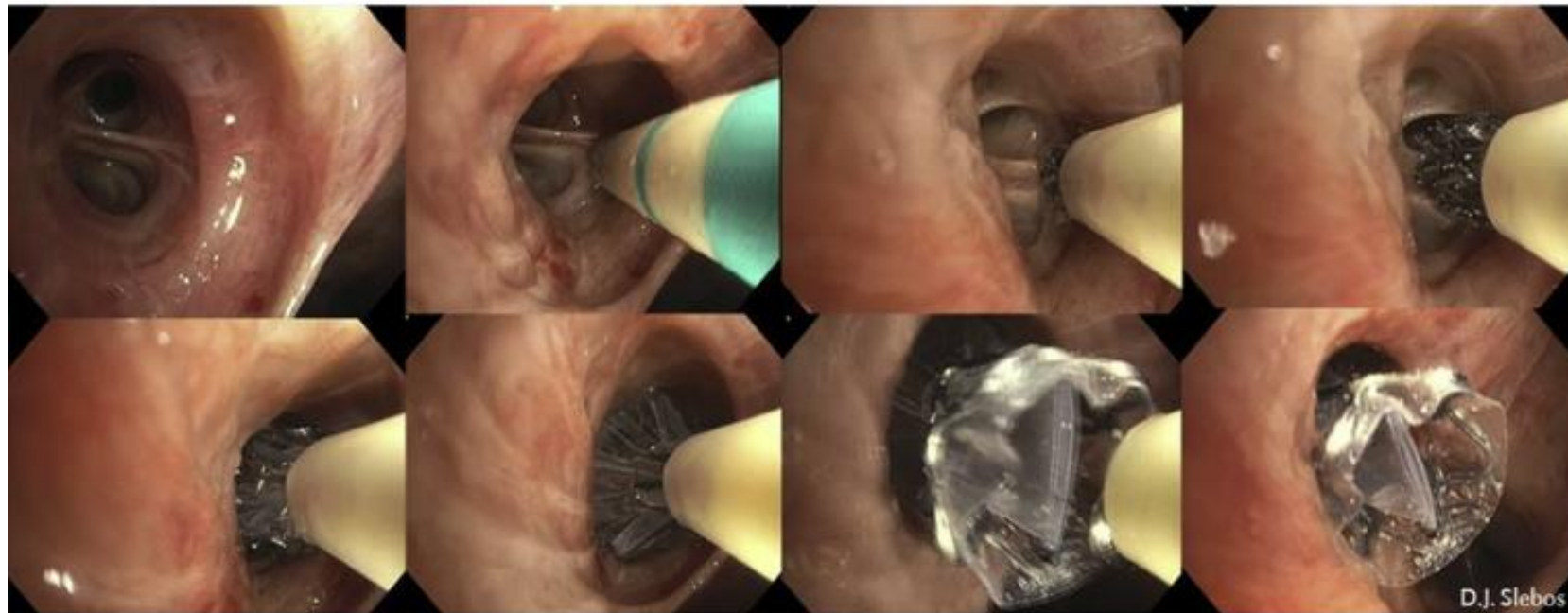
Treatment of severe stable COPD: the multidimensional approach of treatable traits. Van Dijk, ERS, 2020.



Endobronchial Valves for the Treatment of Advanced Emphysema

[Check for updates](#)

Karin Klooster, PhD; and Dirk-Jan Slebos, MD, PhD



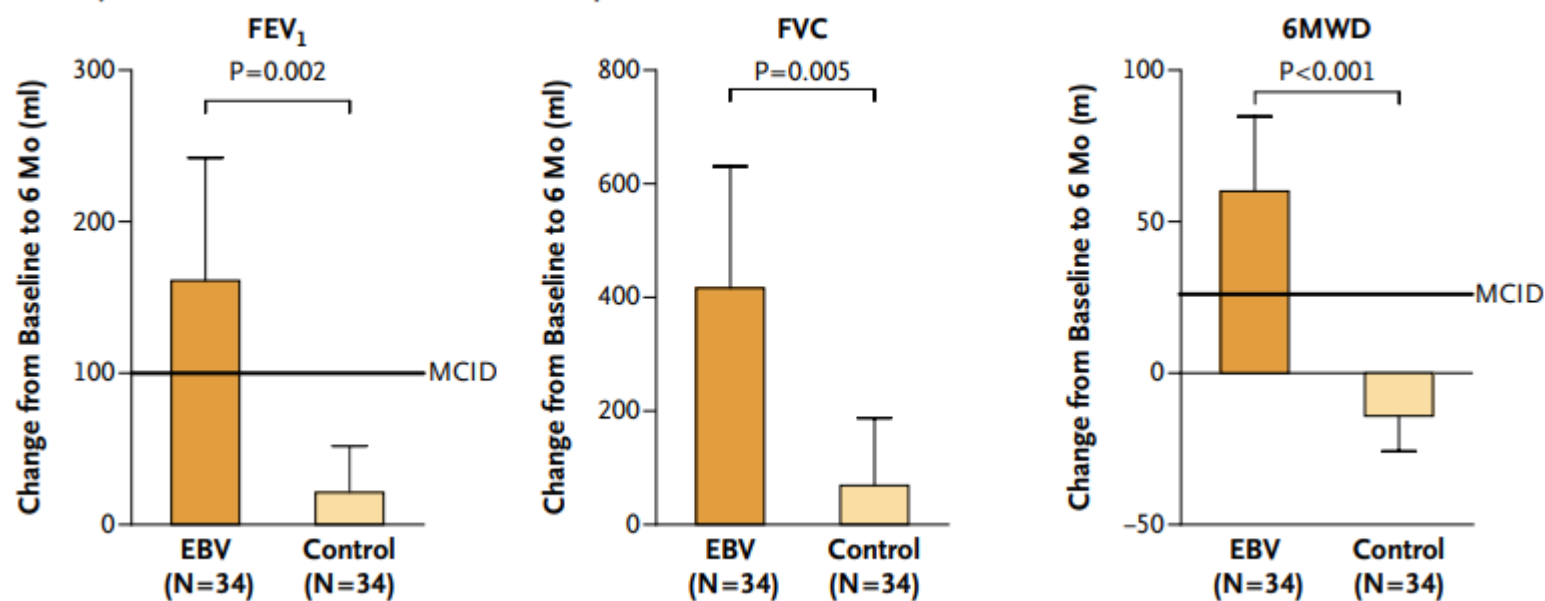
Klooster, K, Endobronchial Valves, CHEST, 2020

ORIGINAL ARTICLE

Endobronchial Valves for Emphysema without Interlobar Collateral Ventilation

Karin Klooster, Nick H.T. ten Hacken, M.D., Ph.D., Jorine E. Hartman, Ph.D.,
Huib A.M. Kerstjens, M.D., Ph.D., Eva M. van Rikxoort, Ph.D.,
and Dirk-Jan Slebos, M.D., Ph.D.

ABSTRACT

A Primary Outcomes in the Intention-to-Treat Population

Endobronchial Valves for the Treatment of

 Check for updates

A



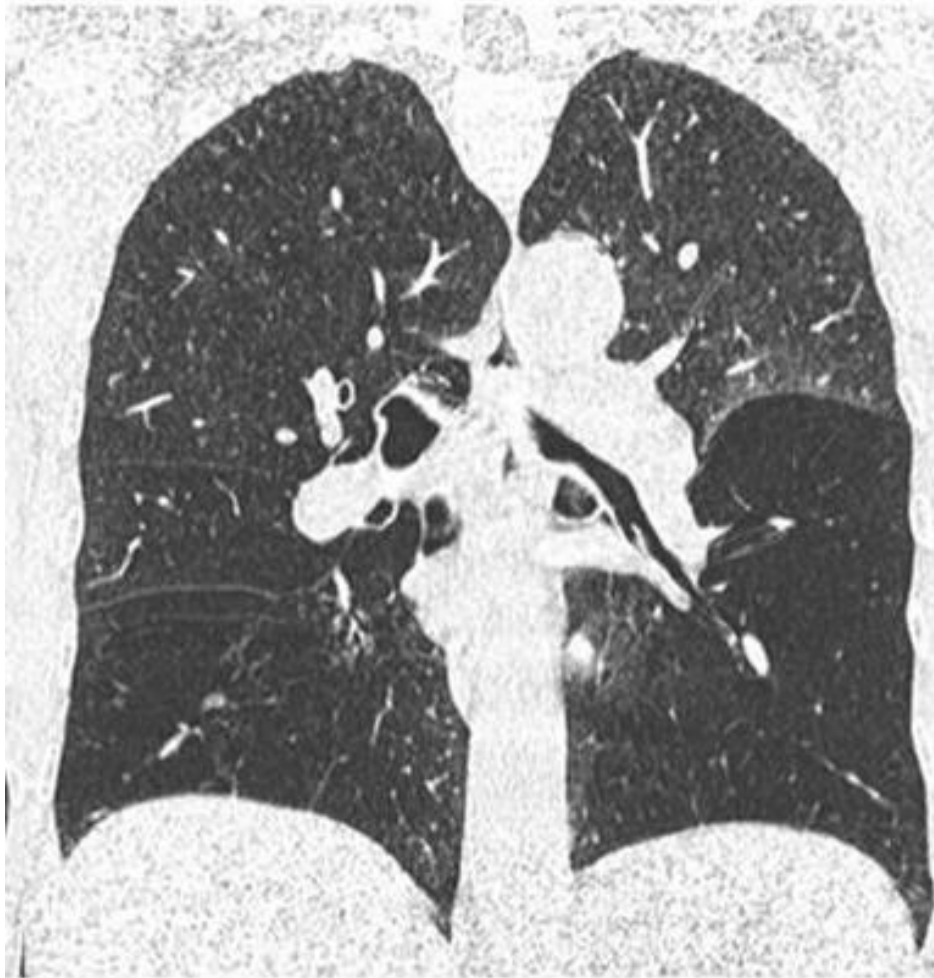
A. Heterogenous emphysema, lower lobe predominant

Endobronchial Valves for the Treatment of Advanced Emphysema

Check for updates

Karin Klooster, PhD, and Dirk-Jan Slebos, MD, PhD

B



- A. Heterogenous emphysema, lower lobe predominant
- B. Expiration phase, air trapping in LLL

Endobronchial Valves for the Treatment of Advanced Emphysema

 Check for updates

Karin Klooster, PhD, and Dirk-Jan Slebos, MD, PhD

C



10

- A. Heterogenous emphysema, lower lobe predominant
- B. Expiration phase, air trapping in LLL
- C. Perfusion scan shows absence of LLL perfusion

Endobronchial Valves for the Treatment of Advanced Emphysema

 Check for updates

Karin Klooster, PhD, and Dirk-Jan Slebos, MD, PhD

C



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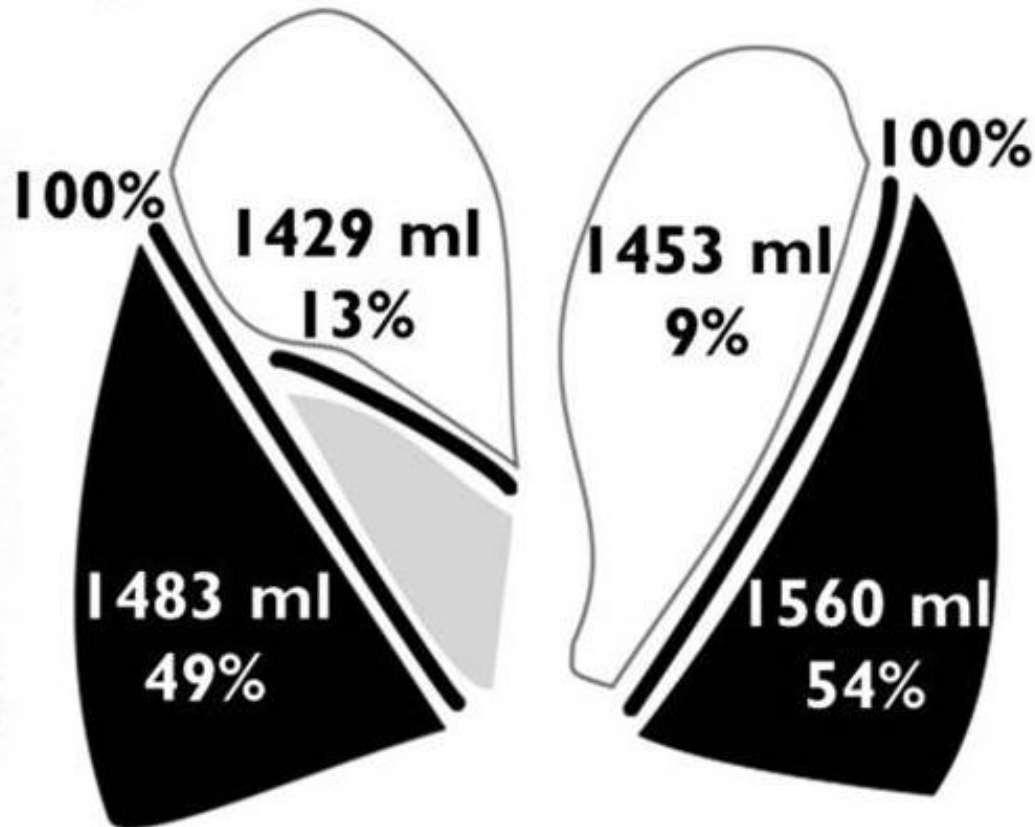
- A. Heterogenous emphysema, lower lobe predominant
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Endobronchial Valves for the Treatment of Advanced Emphysema

[Check for updates](#)

Karin Klooster, PhD, and Dirk-Jan Slebos, MD, PhD

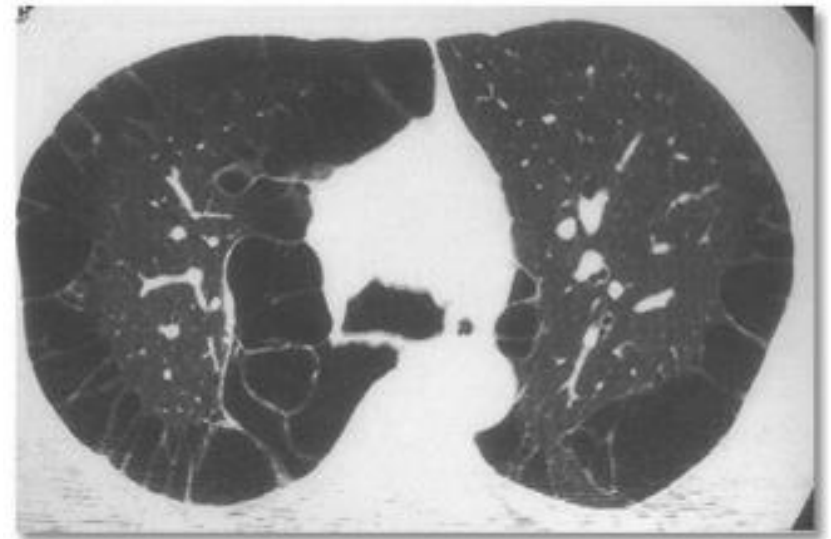
D



- A. Heterogenous emphysema, lower lobe predominant
- B. Expiration phase, air trapping in LLL
- C. Perfusion scan shows absence of LLL perfusion
- D. Quantitative CT scan shows
 - A. emphysema in LLL (and RLL)
 - B. Substantial lobar volume of LLL
 - C. Fissure integrity

The truth about endobronchial valves for COPD

- In the right patient, leads to amazing symptomatic improvement
- Valves are reversible
- Valves generally stay in place
- Hard to find the ideal patient, with no comorbidities
 - No mobility limitations
 - Not on anticoagulation
 - No severe hypoxia or hypercapnea
 - No pulm HTN
 - Low risk for infectious complications
- Must have no collateral ventilation
- Pneumothorax rate (15-25%)



Hour 6: Rapid response on the ward

- 82 F admitted earlier that day for malaise, called to bedside for fevers and hypotension. CXR shows possible RLL infiltrate, has history of frequent UTI-sepsis.
 - What's the latest regarding the SSC (Surviving Sepsis Guidelines).
 - “I want to make sure we're doing everything right ...”



[SCCM](#) > [Clinical Resources](#) > [Guidelines](#) > [All SCCM Guidelines](#) > [Adult SSC Guidelines](#)

GUIDELINES

SEPSIS

Surviving Sepsis Campaign Guidelines 2021

PUBLISHED: 10/4/2021

Critical Care Medicine: October 4, 2021

Key questions

Key Question	Options	Answer
Fluid bolus, what to give?	Normal saline versus balanced (e.g. lactated Ringer's)	No difference in mortality*
Fluids, how fast to give?	999 mL/hr versus 333 ml/hr	No difference in mortality
Antibiotics, when to start?	Within 1 st hour of suspicion	Improved mortality, but only observational data
Steroids, when to start?	Hydrocortisone, fludrocortisone	Improved 90d mortality*
Serial labs, such as lactate?	Lactate every 6 hours, or until downtrending	No difference in mortality*
Do protocols help?	Before/after SEP-1 mandate	No difference in mortality
Pressors and route of admin	PIV versus central line	Weak recommendation

* Some conflicting results

Normal Saline vs. LR (2018)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Balanced Crystalloids versus Saline in Critically Ill Adults

Matthew W. Semler, M.D., Wesley H. Self, M.D., M.P.H.,
Jonathan P. Wanderer, M.D., Jesse M. Ehrenfeld, M.D., M.P.H.,
Li Wang, M.S., Daniel W. Byrne, M.S., Joanna L. Stollings, Pharm.D.,
Avinash B. Kumar, M.D., Christopher G. Hughes, M.D.,
Antonio Hernandez, M.D., Oscar D. Guillamondegui, M.D., M.P.H.,
Addison K. May, M.D., Liza Weavind, M.B., B.Ch., Jonathan D. Casey, M.D.,
Edward D. Siew, M.D., Andrew D. Shaw, M.B., Gordon R. Bernard, M.D.,
and Todd W. Rice, M.D., for the SMART Investigators

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Balanced Crystalloids versus Saline in Noncritically Ill Adults

Wesley H. Self, M.D., M.P.H., Matthew W. Semler, M.D.,
Jonathan P. Wanderer, M.D., Li Wang, M.S., Daniel W. Byrne, M.S.,
Sean P. Collins, M.D., Corey M. Slovis, M.D., Christopher J. Lindsell, Ph.D.,
Jesse M. Ehrenfeld, M.D., M.P.H., Edward D. Siew, M.D.,
Andrew D. Shaw, M.B., Gordon R. Bernard, M.D.,
and Todd W. Rice, M.D., for the SALT-ED Investigators*

Composite outcome

- 14.3% (balanced), 15.4% (NS)
- $p=0.04$

No benefit

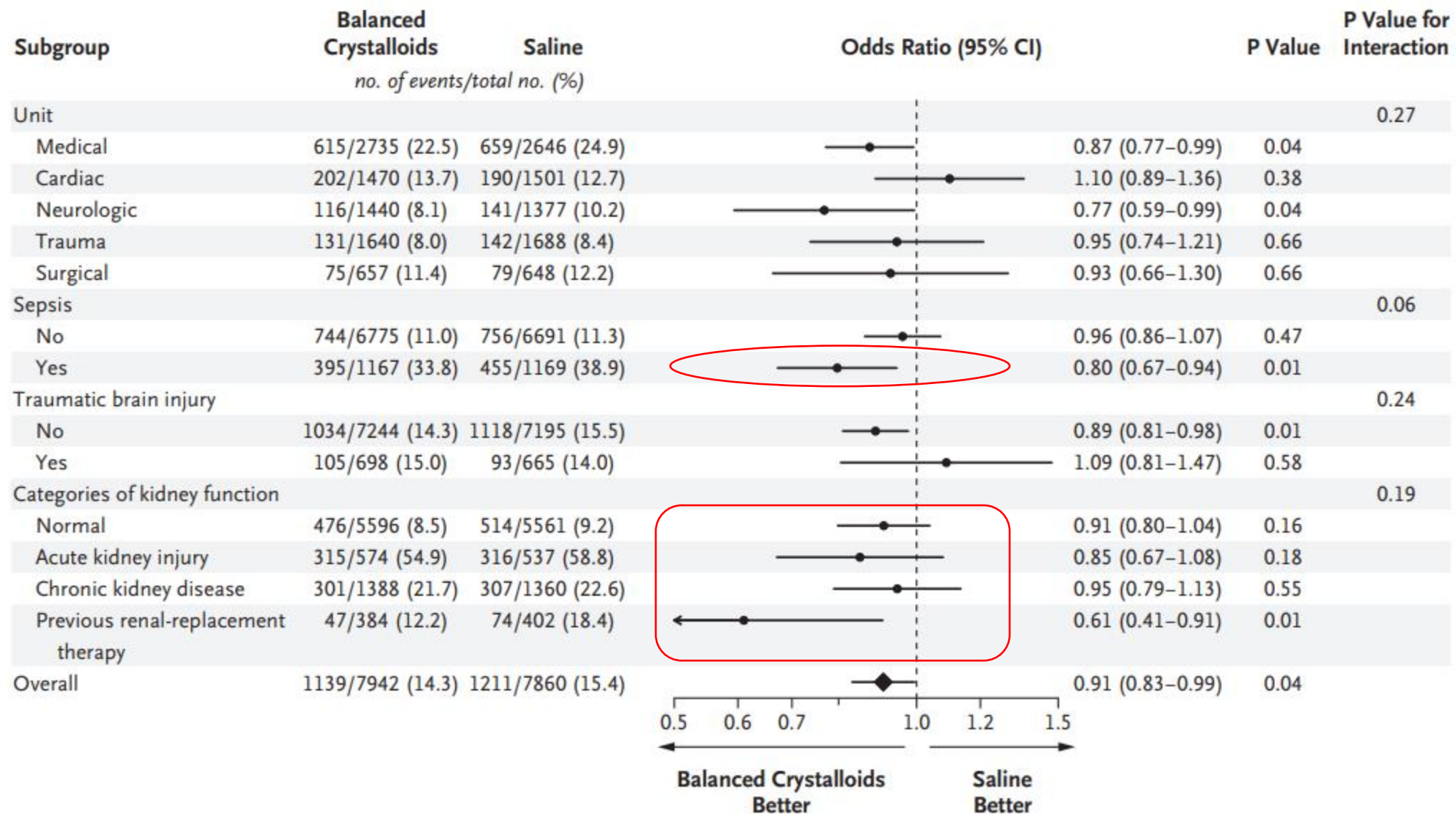


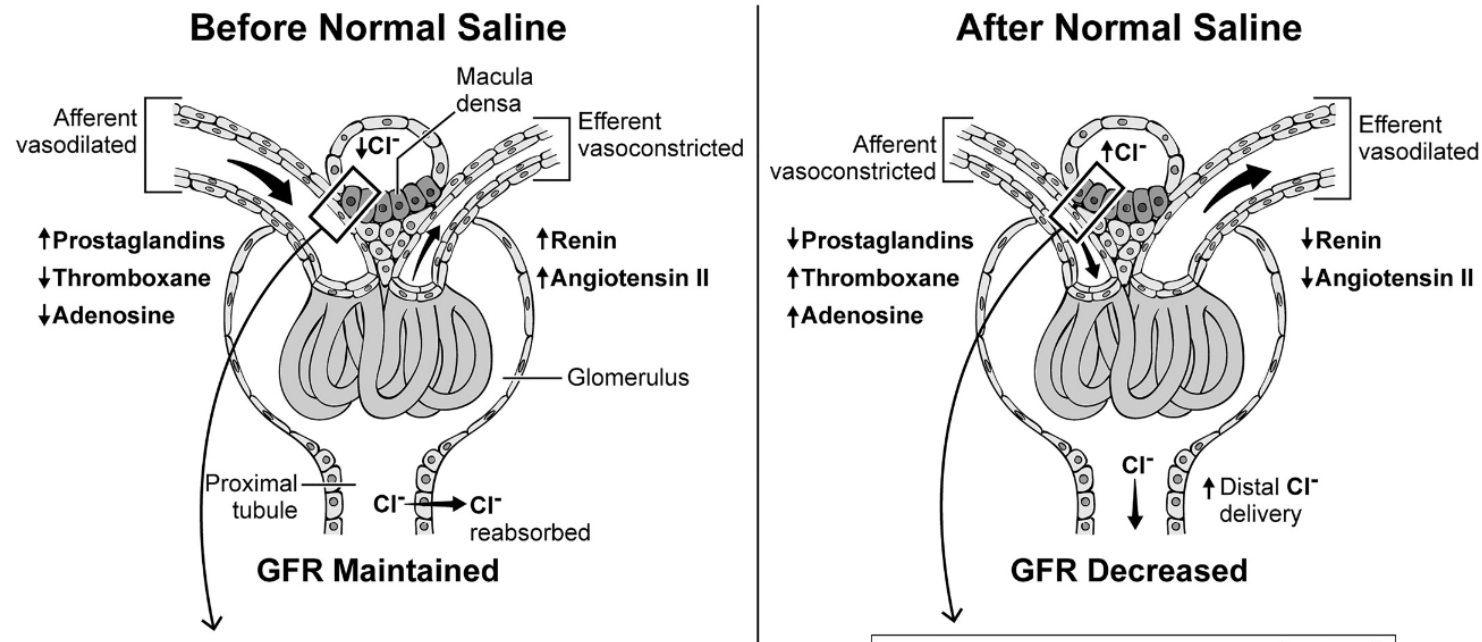
Figure 3. Subgroup Analysis of Rates for the Composite Outcome of Death, New Receipt of Renal-Replacement Therapy, or Persistent Renal Dysfunction.

Evils of Chloride

CHLORIDE AND ACUTE KIDNEY INJURY

F595

TGF During Hypoperfusion



- Increases afferent vasoconstriction, leading to decreased GFR.
- Also acts on smooth muscle cells in mesangial cells
- Increased edema also reduces capillary blood flow to kidneys

Original Investigation

August 10, 2021

Effect of Intravenous Fluid Treatment With a Balanced Solution vs 0.9% Saline Solution on Mortality in Critically Ill Patients

The BaSICS Randomized Clinical Trial

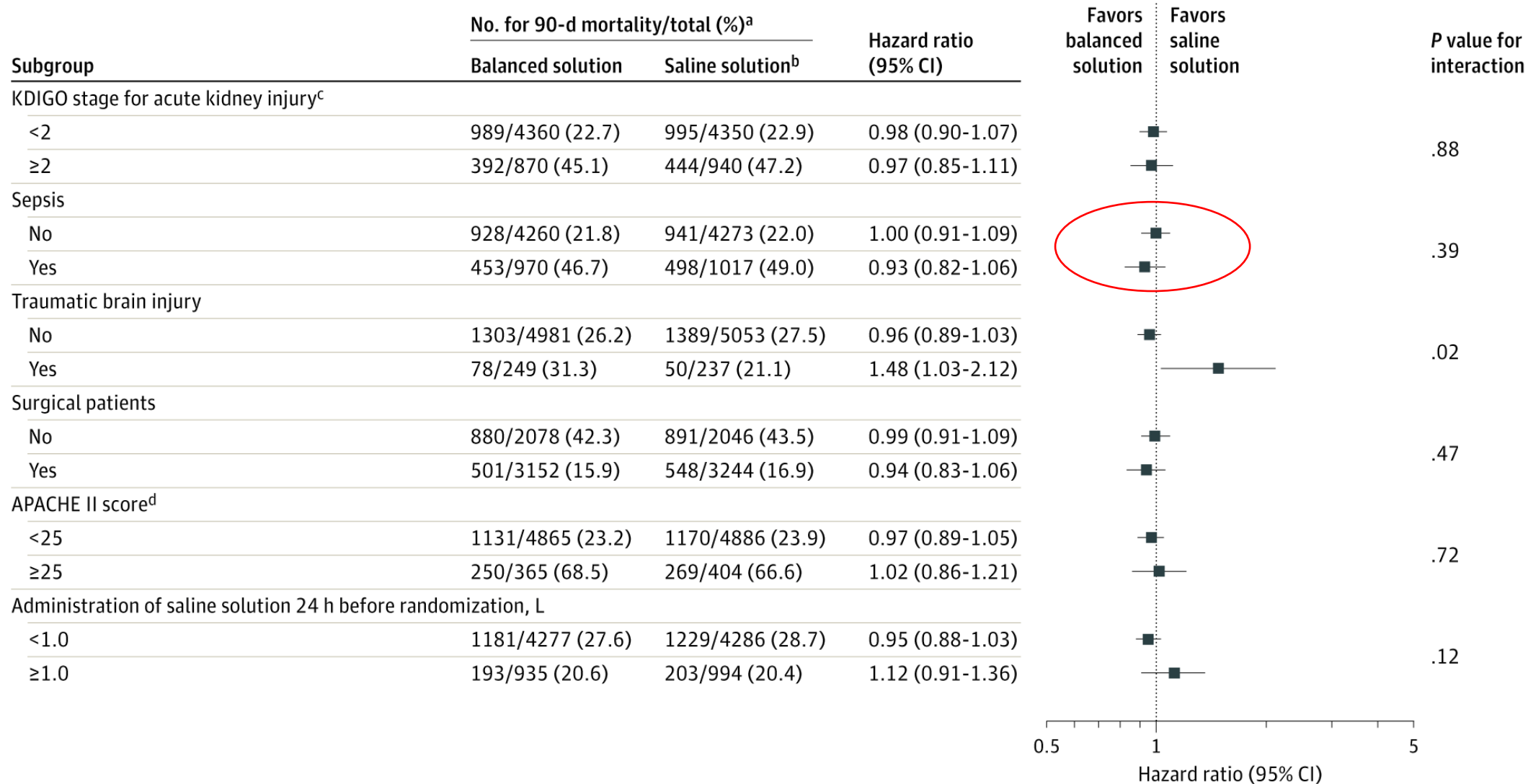
Fernando G. Zampieri, MD, PhD^{1,2}; Flávia R. Machado, MD, PhD^{2,3}; Rodrigo S. Biondi, MD^{2,4}; [et al](#)

[» Author Affiliations](#) | [Article Information](#)

JAMA. 2021;326(9):818-829. doi:10.1001/jama.2021.11684

90 day mortality

- 26.4% (balanced) versus 27.2% (NS), $p=0.47$



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MARCH 3, 2022

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Balanced Multielectrolyte Solution versus Saline in Critically Ill Adults

Simon Finfer, M.D., Sharon Micallef, B.N., Naomi Hammond, Ph.D., Leanlove Navarra, B.S.N.,
Rinaldo Bellomo, M.D., Ph.D., Laurent Billot, M.Res., Anthony Delaney, M.D., Ph.D.,
Martin Gallagher, M.D., Ph.D., David Gattas, M.D., Qiang Li, M.Biostat., Diane Mackle, M.N.,
Jayanthi Mysore, M.S., Manoj Saxena, M.D., Ph.D., Colman Taylor, Ph.D., Paul Young, M.D., Ph.D.,
and John Myburgh, M.D., D.Sc., for the PLUS Study Investigators and the Australian
and New Zealand Intensive Care Society Clinical Trials Group*

ABSTRACT

BACKGROUND

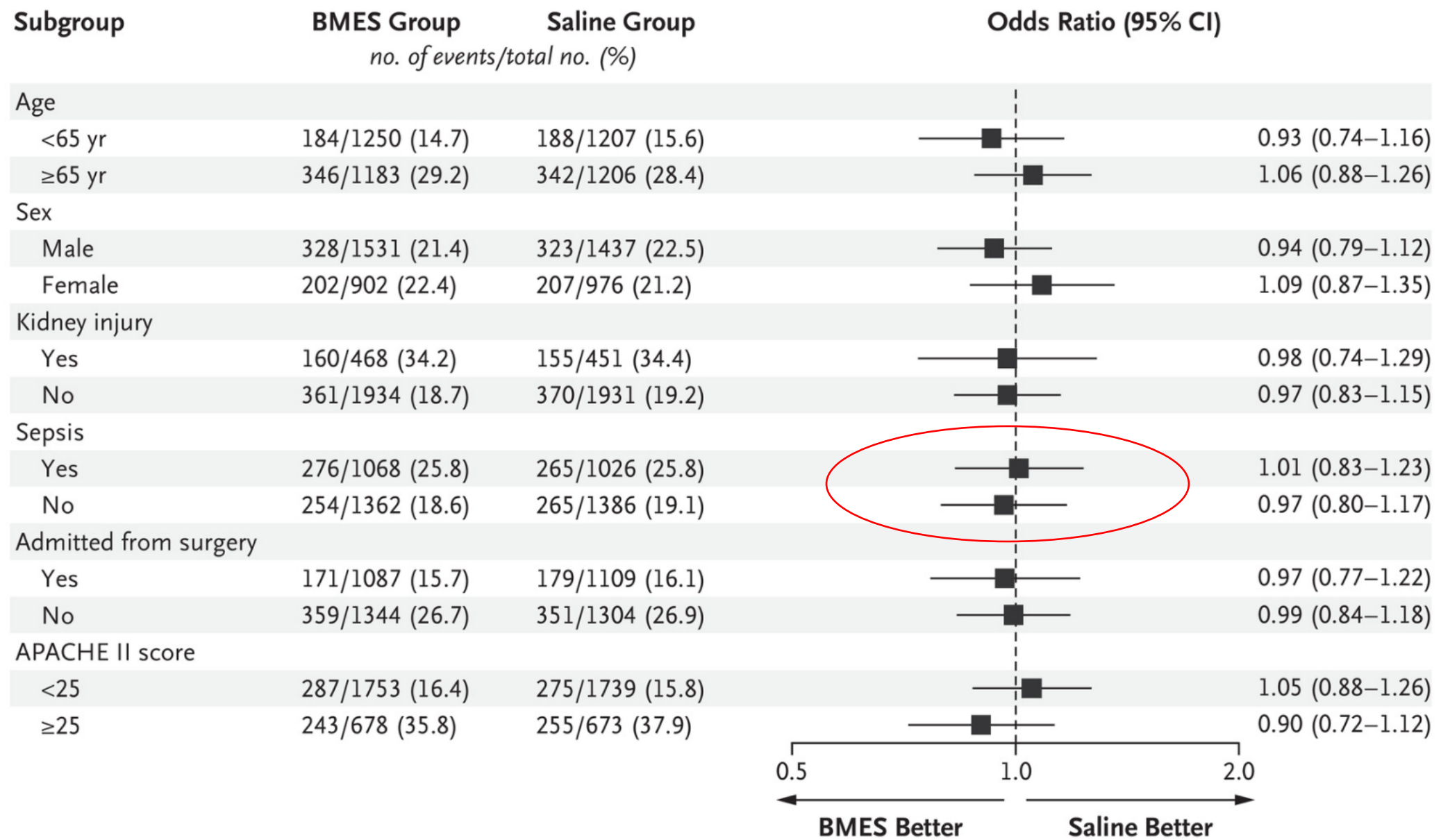
Whether the use of balanced multielectrolyte solution (BMES) in preference to 0.9% sodium chloride solution (saline) in critically ill patients reduces the risk of acute kidney injury or death is uncertain.

The authors' affiliations are listed in the Appendix. Dr. Finfer can be contacted at sfinfer@georgeinstitute.org.au or at the George Institute for Global Health, 1 King

90 day mortality

- 21.8% (balanced fluids) versus 22.0% (NS), $p=0.90$

B Subgroup Analysis of Death from Any Cause



Comparison of trials

	SPLIT (2015)	SMART (2018)	BaSICS (2021)	PLUS (2022)
Patients	2,278	15,808	11,052	5,037
Sites	4 sites	Single center	75 sites	53 sites
Study characteristics	Blinded	Unblinded	Blinded	Blinded
90 d mortality in balanced fluids	7.6%	10.3%	26.4%	21.8%
Mechanical ventilation	69%	34%	44%	76%
Clinical benefit?	No	Yes, composite outcome	No	No

ORIGINAL ARTICLE

Balanced Crystalloids versus Saline in Critically Ill Adults — A Systematic Review with Meta-Analysis

Naomi E. Hammond, Ph.D.^{1,2}, Fernando G. Zampieri, Ph.D.^{3,4}, Gian Luca Di Tanna, Ph.D.⁵, Tessa Garside, Ph.D.^{1,2}, Derick Adigbli, Ph.D.^{1,2}, Alexandre B. Cavalcanti, M.D. Ph.D.³, Flavia R. Machado, M.D., Ph.D.⁶, Sharon Micallef, B.N.¹, John Myburgh, Ph.D.^{1,7}, Mahesh Ramanan, M.Med.^{8,9}, Todd W. Rice, M.D.¹⁰, Matthew W. Semler, M.D.¹⁰, Paul J. Young, Ph.D.^{11,12}, Balasubramanian Venkatesh, M.D.^{1,13}, Simon Finfer, M.D.^{1,14}, and Anthony Delaney, Ph.D.^{1,2}

Drs. Hammond and Zampieri, as well as Drs. Finfer and Delaney, contributed equally to this article.

CONCLUSIONS The estimated effect of using balanced crystalloids versus saline in critically ill adults ranges from a 9% relative reduction to a 1% relative increase in the risk of death, with a high probability that the average effect of using balanced crystalloids is to reduce mortality.

Hour 9: The vaper

- 24 F with hx of asthma, was brought in by medics in respiratory distress. Turning around with nebs, IV solumedrol, and NIPPV. Reportedly vapes daily.
- “What can vaping do to your lungs?”



EVALI

- E-cigarettes
 - Delivers: nicotine, THC, CBD, butane hash oils, flavoring
 - Toxins: propylene glycol, diacetyl, acrolein
- E-cigarette Ventilator Associated Lung Injury

ORIGINAL ARTICLE

Pulmonary Illness Related to E-Cigarette Use in Illinois and Wisconsin — Final Report

Jennifer E. Layden, M.D., Ph.D., Isaac Ghinai, M.B., B.S., Ian Pray, Ph.D., Anne Kimball, M.D., Mark Layer, M.D., Mark W. Tenforde, M.D., Ph.D., Livia Navon, M.S., Brooke Hoots, Ph.D., Phillip P. Salvatore, Ph.D., Megan Elderbrook, M.P.H., Thomas Haupt, M.S., Jeffrey Kanne, M.D., Megan T. Patel, M.P.H., Lori Saathoff-Huber, M.P.H., Brian A. King, Ph.D., M.P.H., Josh G. Schier, M.D., Christina A. Mikosz, M.D., M.P.H., and Jonathan Meiman, M.D.

ABSTRACT

BACKGROUND

E-cigarettes are battery-operated devices that heat a liquid and deliver an aerosolized product to the user. Pulmonary illnesses related to e-cigarette use have been reported, but no large series has been described. In July 2019, the Wisconsin Department of Health Services and the Illinois Department of Public Health received

From the
Health,
M.T.P.,
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Epidemiol

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

APRIL 23, 2020

VOL. 382 NO. 17

Hospitalizations and Deaths Associated with EVALI

A.K. Werner, E.H. Koumans, K. Chatham-Stephens, P.P. Salvatore, C. Armatas, P. Byers, C.R. Clark, I. Ghinai, S.M. Holzbauer, K.A. Navarette, M.L. Danielson, S. Ellington, E.D. Moritz, E.E. Petersen, E.A. Kiernan, G.T. Baldwin, P. Briss, C.M. Jones, B.A. King, V. Krishnasamy, D.A. Rose, and S. Reagan-Steiner, for the Lung Injury Response Mortality Working Group*

ABSTRACT

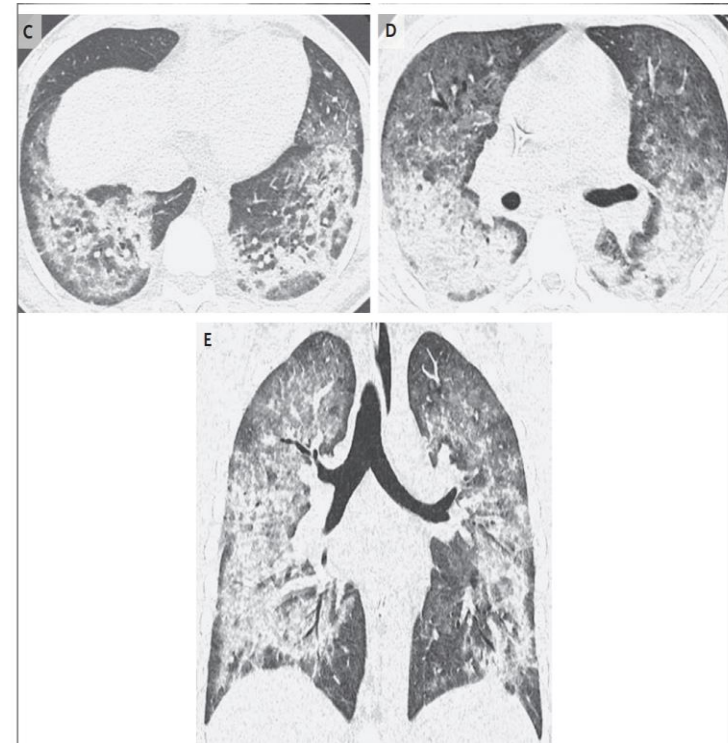
BACKGROUND

As of January 7, 2020, a total of 2558 hospitalized patients with nonfatal cases and 60 patients with fatal cases of e-cigarette, or vaping, product use–associated lung injury (EVALI) had been reported to the Centers for Disease Control and Prevention (CDC).

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Werner at the Centers for Disease Control and Prevention, 4770 Buford Hwy., MS S106-6, Atlanta, GA 30341, or

EVALI

- 98 patients in Wisconsin 2019-2020.
- Case definition:
 - E-cigarette use < 90 days prior
 - Pulmonary infiltrates
 - Absence of infection (minimum, neg resp viral PCR)
 - Absence of alternative explanation (e.g. pulm edema)
- Symptom onset ~ 6 days prior
- Bronchoalveolar lavage
 - Typical neutrophilic cell count (no eosinophils)
- Treatment: Supportive care
- Over half of deaths were seen in clinic prior to hospitalization (Werner, et al)



Hour 11: The vapor → asthmatic

- CXR and CT scan are clear. This is asthma.
- Vaping was just a rumor.
- “What’s new for asthma?”



Biologics

- Indicated for severe asthmatics, refractory to maximal medical therapy:
 - ICS/LABA
 - Adequate environmental control (including no smoking)
 - Monteleukast
 - Antihistamine

Agents

	Route, Dose	Forms	Mechanism	Indications
Omalizumab (Xolair)	SQ 75-375mg Q2-4 weeks	Prefilled syringe	Elevated IgE	Asthma (high IgE) Chronic idiopathic urticaria
Mepolizumab (Nucala)	SQ 100mg Qmonth	Prefilled syringe, autoinjector pen	Anti-eosinophil, via IL-5	Eosinophilic Asthma EGPA (Churg-Straus) HIES
Dupilumab (Dupixent)	SQ 600mg load SQ 300mg Q2 wks	Prefilled syringe, autoinjector pen	IL-4 and IL 13 blocker	Eosinophilic Asthma Steroid-dependent asthma Chronic rhinosinusitis with nasal polyposis Atopic dermatitis
Benralizumab (Fasenra)	SQ 30mg Q4 wks x 3 then 30mg Q8wks	Prefilled syringe, autoinjector pen	IL-5Ra Ab	Eosinophilic asthma
Reslizumab (Cinqair)	IV 3mg/kg Q4 wks	IV infusion	IL-5 Ab	Eosinophilic asthma
Tezepelumab (Tezspire)	SQ 210mg Q4 wks	Prefilled syringe	TSLP	Severe asthma

B Secondary Oral Glucocorticoid End Points, According to Blood Eosinophil Subgroup

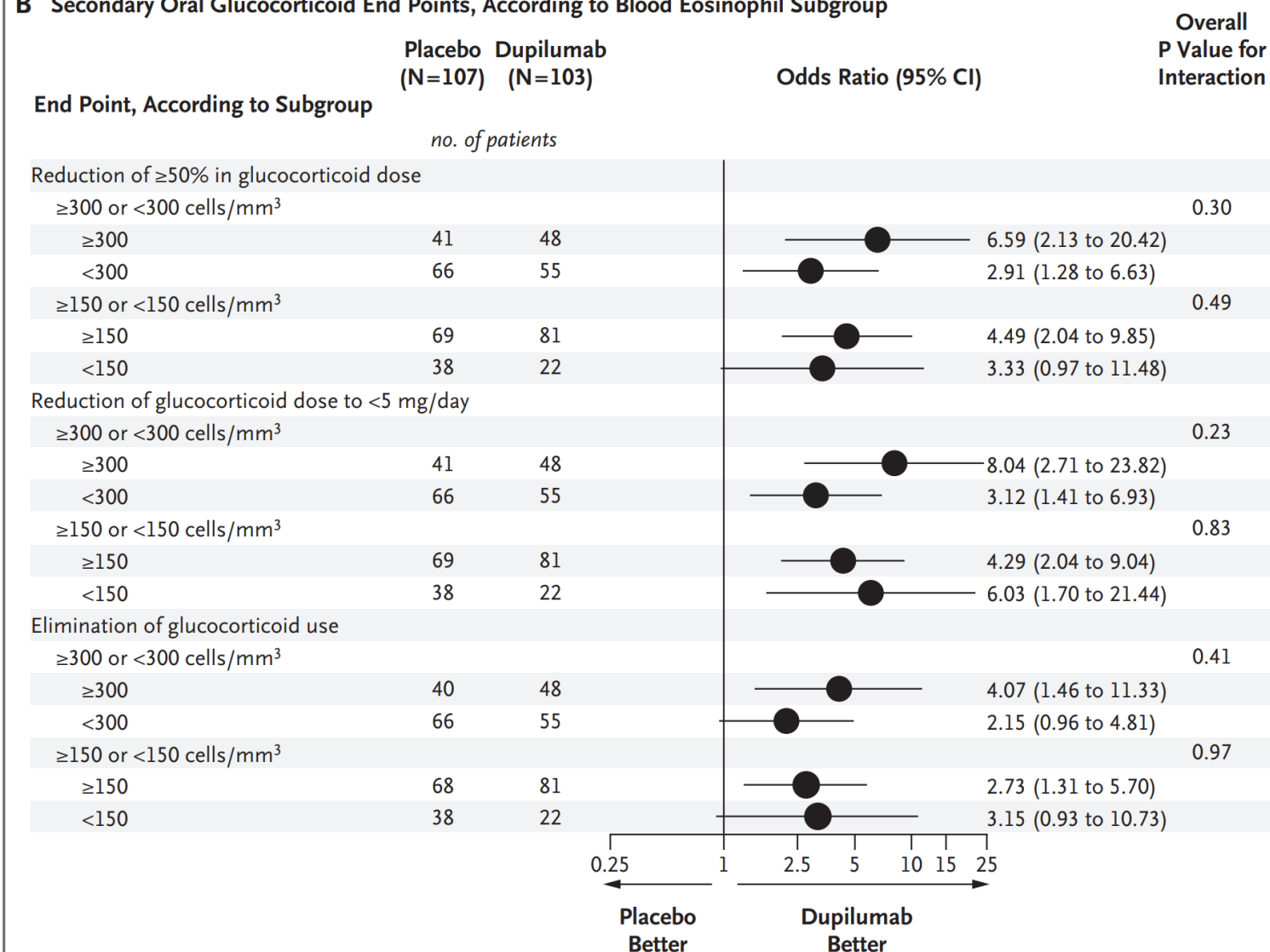
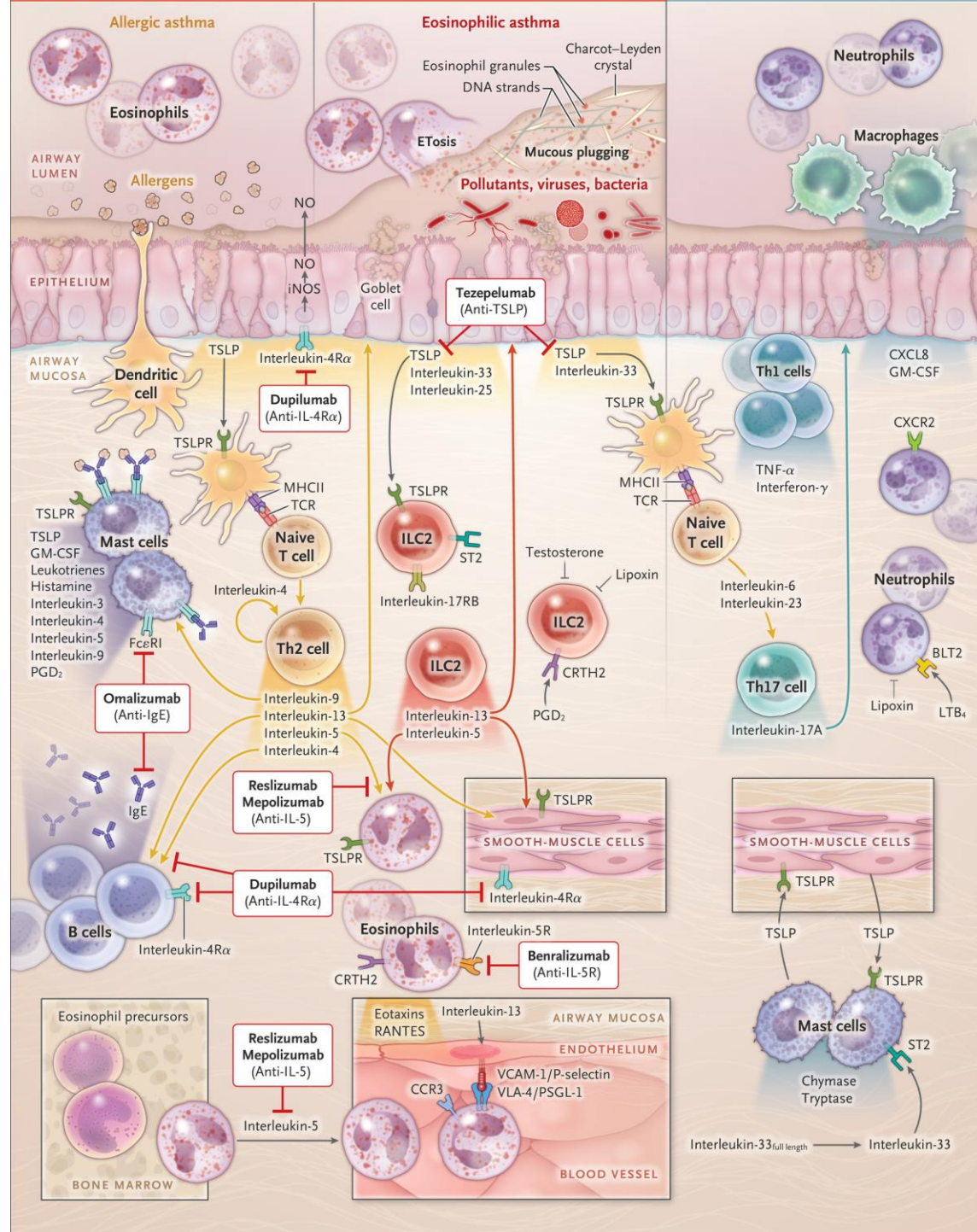


Figure 2. Primary End Point and Secondary Oral Glucocorticoid End Points at Week 24, According to Baseline Blood Eosinophil Subgroup.

A Type 2-High Asthma

B Type 2–Low Asthma



Your shift is over



WE ARE *Valley*

In review

- TTM2 confirmed the results of TTM1, which did not show benefit with cooling versus normothermia in cardiac arrest that was seen with Hyperion, HACA, and Bernard.

- Whether you choose to cool depends on



- Endobronchial valves for COPD can provide significant symptomatic benefit (FEV1 150cc, 6MWT 50m) in end-stage COPD, in the right patient.

In review

- The BaSICS and PLUS trial did not show mortality benefit with balanced fluids (LR) over normal saline in critically ill patients.
 - NEJM Systematic Review thinks there might be clinical benefit
 - SCCM: weak recommendation for balanced, very low evidence of quality
- EVALI (E-cigarette Ventilator Associated Lung Injury) is defined as pulm infiltrates and acute hypoxia associated with E-cigarette use within last 90 days and no alternative explanation.
 - Often a subacute presentation
- Biologics are a very successful therapeutic modality for severe asthmatics, with elevated IgE and eosinophil levels, or steroid dependency.
 - Is your patient T2 high or T2 low phenotype?



Topics that didn't make the cut this year

- Lung cancer screening – new CMS eligibility criteria
- GINA 2021 asthma guidelines
- New 2022 IPF guidelines from ATS
 - New agents for IPF
 - PPF
 - Cryobiopsy
- Septic shock and dynamic measurement of volume status
- Steroids for septic shock/ARDS
- Immunotherapy for lung cancer, and side effects
- VILI and SILI



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