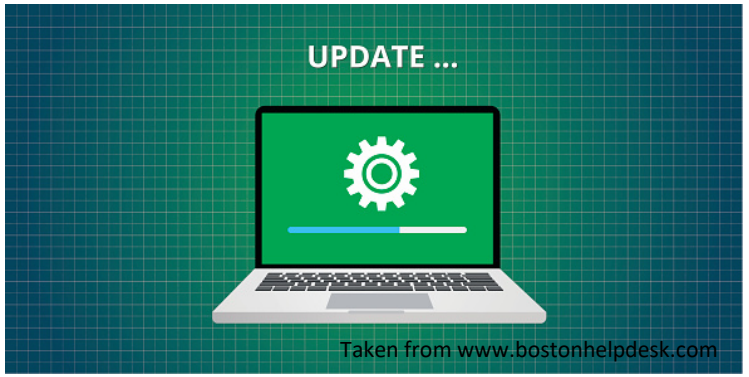
WA ACP Pulmonary/Critical Care Updates 2022



Richard Kim, MD
Valley Medical Center

WE ARE Valley

Relevant Disclosures

- None

You’re on call

Taken from Houston Chronicle website

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

2002 HACA
- VF/VT
- N=275
- Improved survival

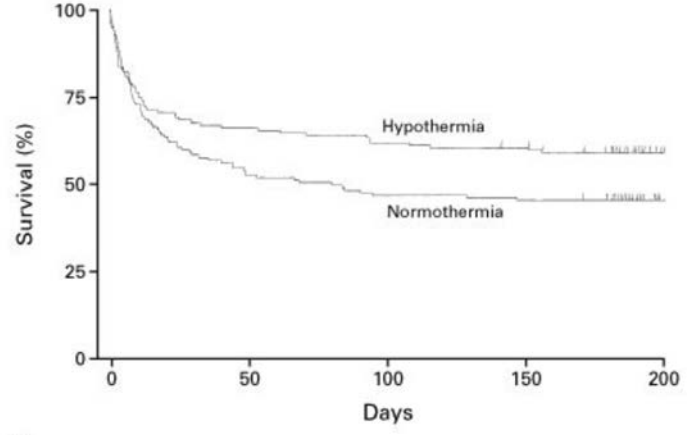
2002 Bernard
- VF/VT
- N=77
- Improved outcomes

2013 TTM
- VF/VT, PEA, asystole
- N=939
- No difference 33C v. 36C

2019 HYPERION
- PEA/asystole
- N=581
- Improved survival + performance status (10.2% vs. 5.7%)

2021 TTM2
- VF/VT, PEA, asystole
- N=1,861
- No difference 33C v. 36C

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



No. at Risk					
Hypothermia	137	92	86	83	11
Normothermia	138	74	66	64	9

Censored data are indicated by tick marks.

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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

2002 HACA

VF/VT

N=275

Improved survival

2002 Bernard

VF/VT

N=77

Improved outcomes

2013 TTM

VF/VT, PEA, asystole

N=939

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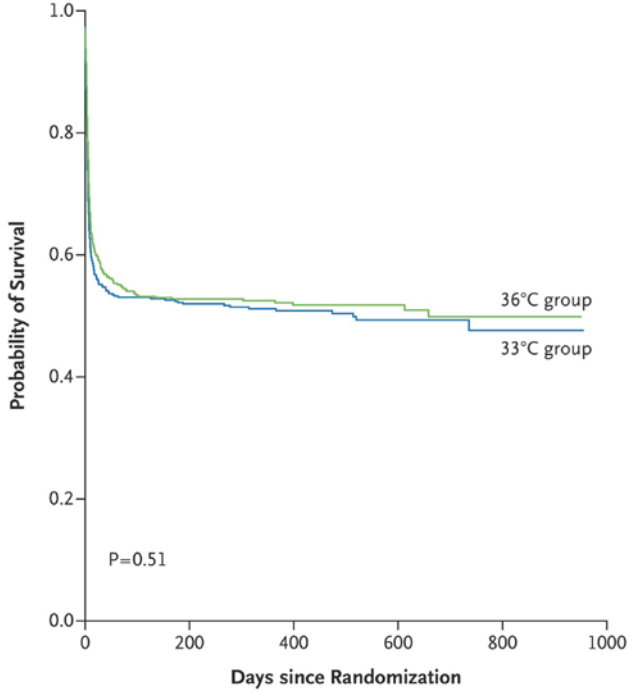

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Figure 3. Distribution of Cerebral Performance Category Scores on Day 90 after Randomization.

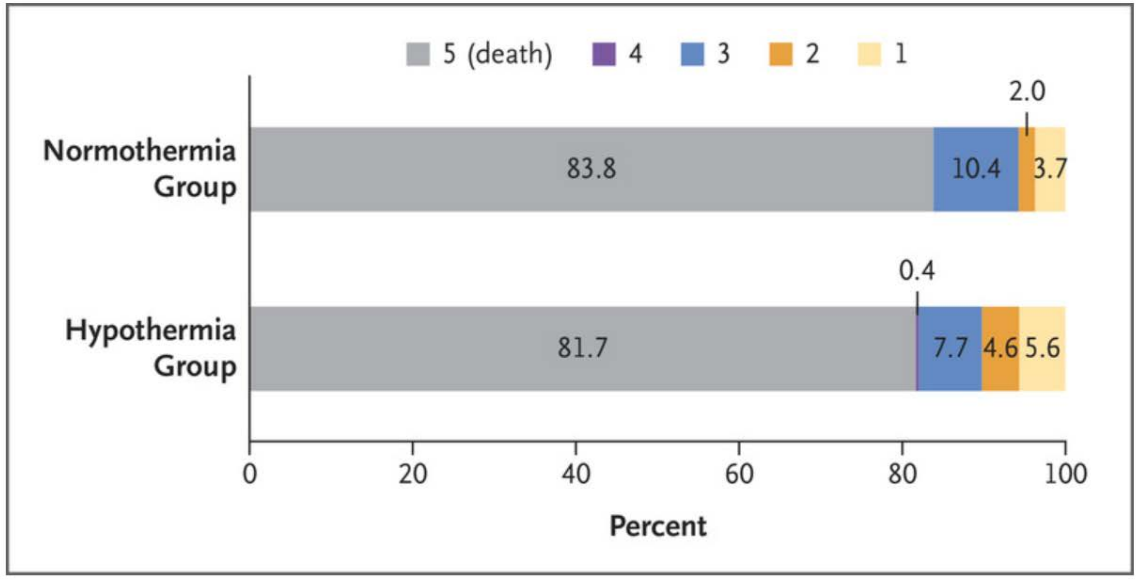

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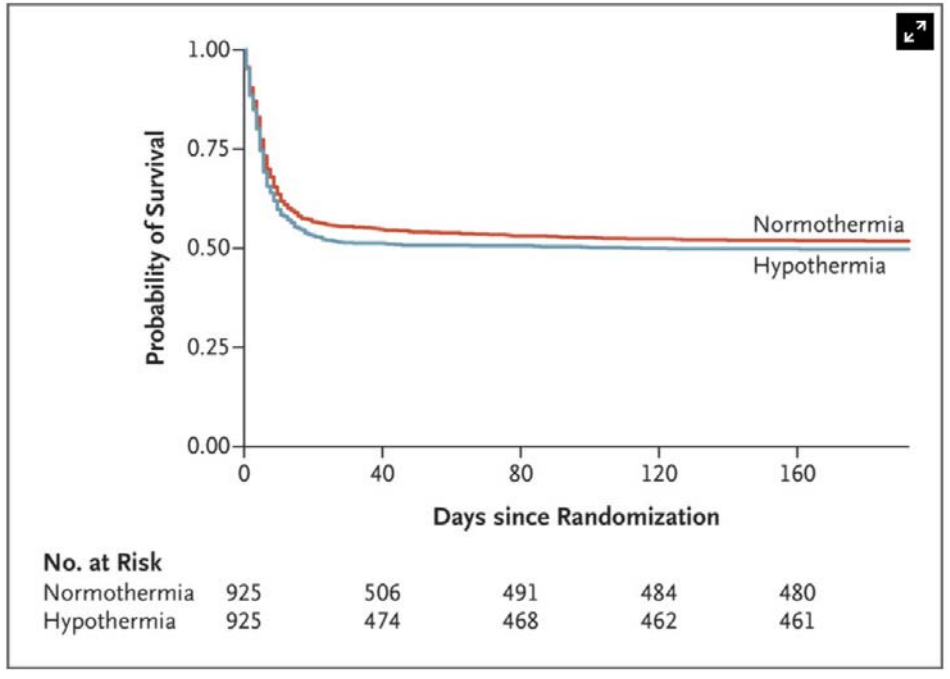
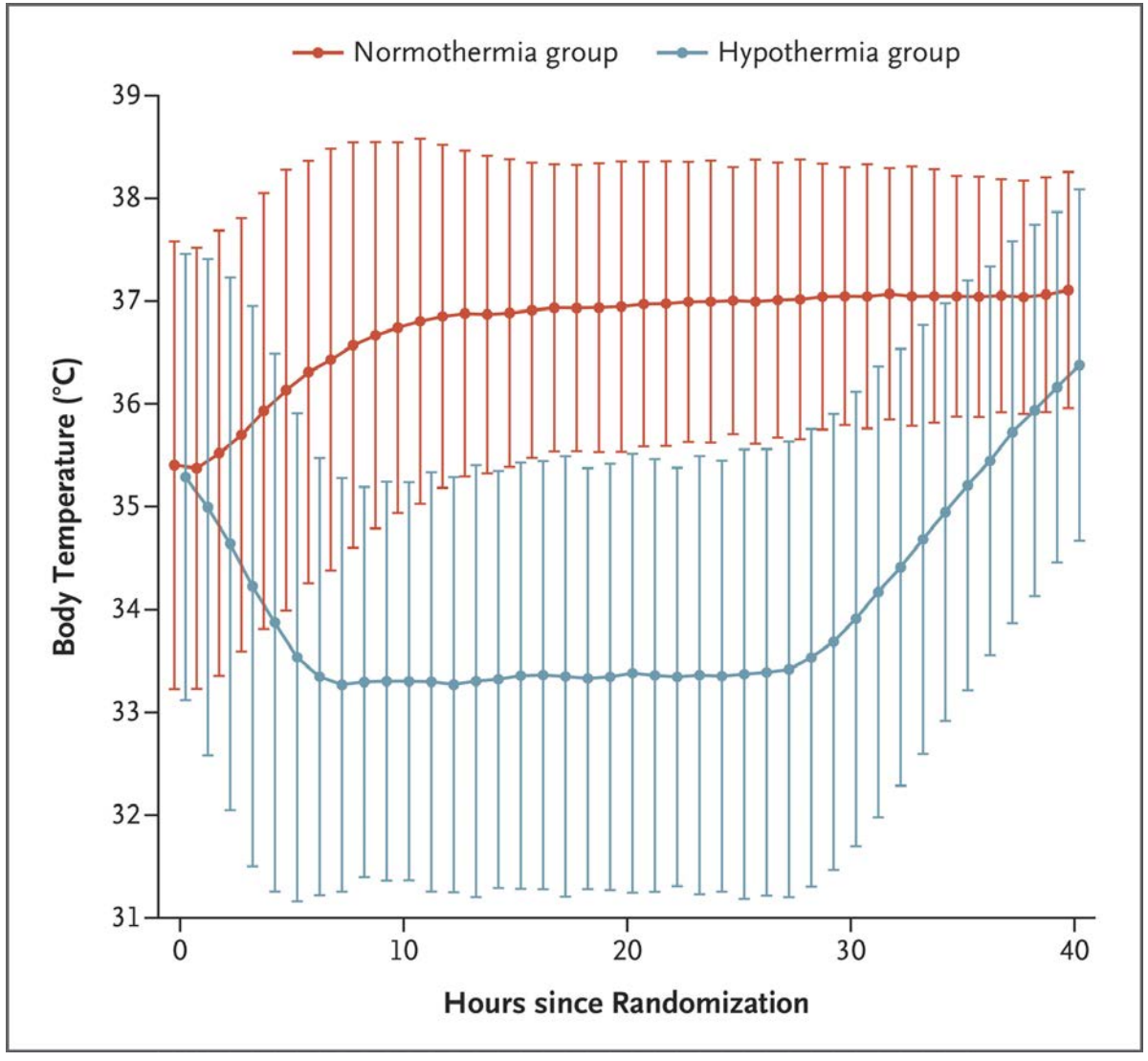
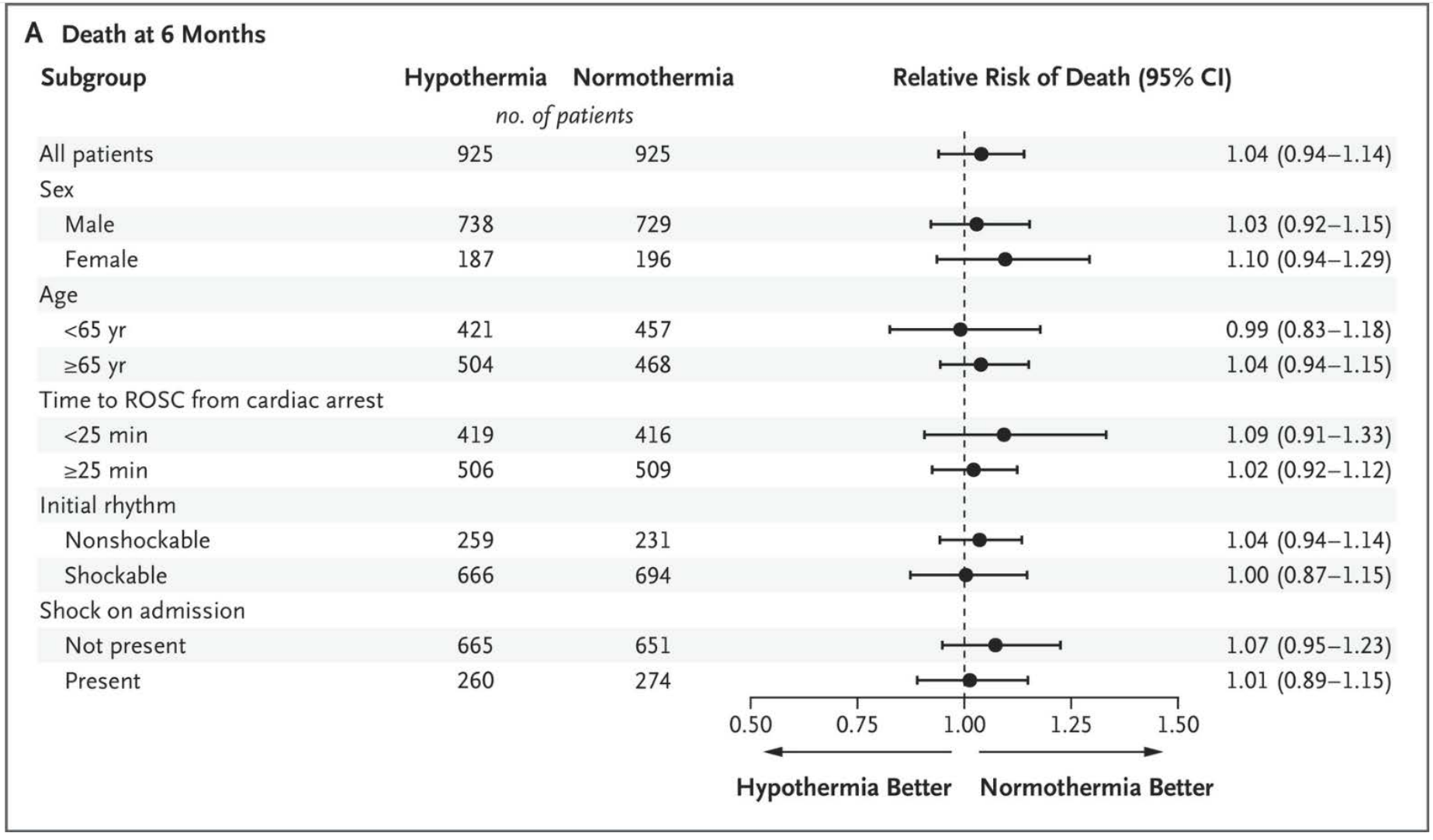
Figure 3. Probability of Survival until 180 Days after Randomization.



TTM2


Normothermia group
Hypothermia group
Body Temperature (°C)
39
38
37
36
35
34
33
32
31
0
10
20
30
40
Hours since Randomization

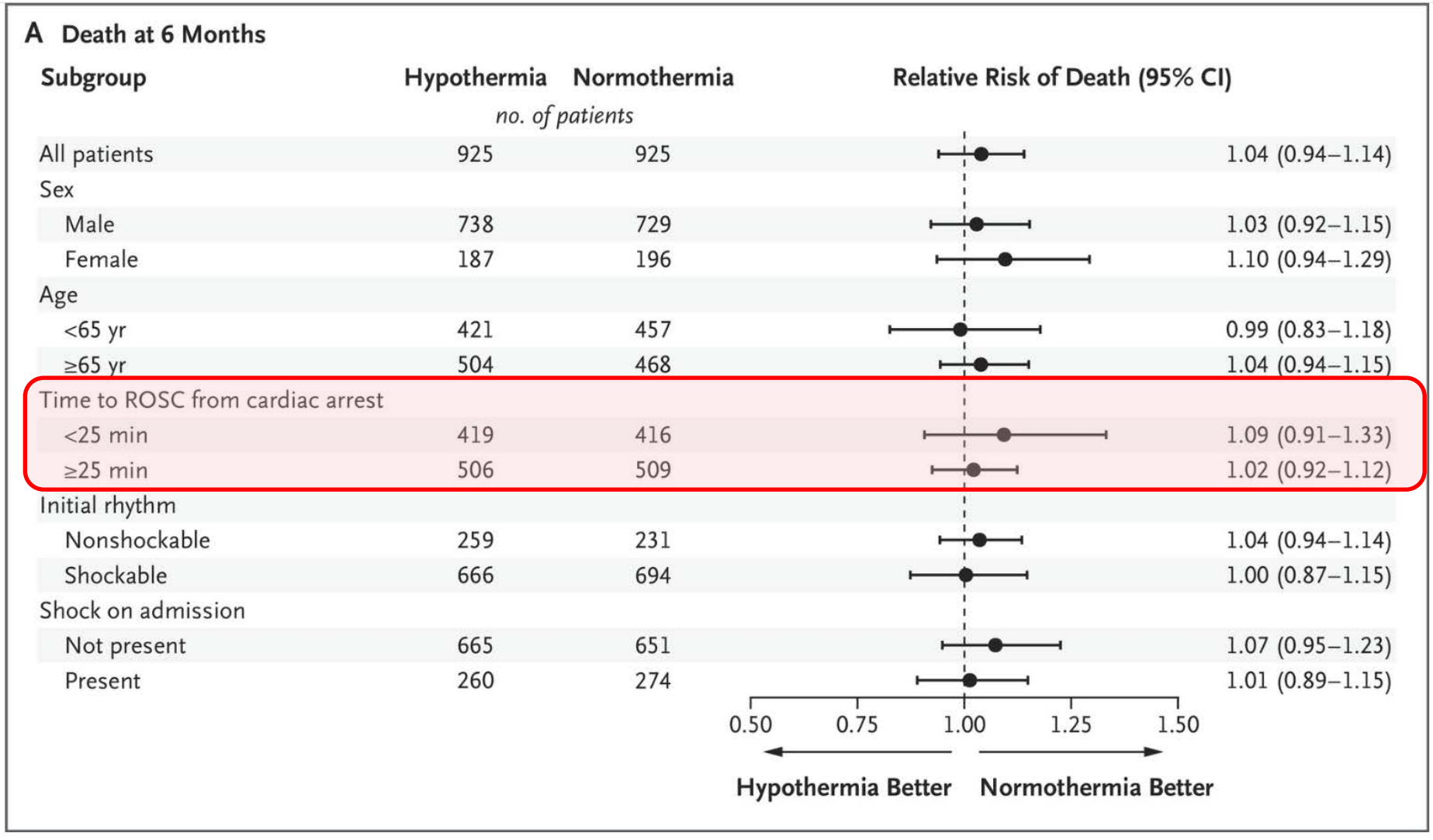
TTM2



A Death at 6 Months

Subgroup	Hypothermia	Normothermia	Relative Risk of Death (95% CI)
	no. of patients		
All patients	925	925	1.04 (0.94–1.14)
Sex			
Male	738	729	1.03 (0.92–1.15)
Female	187	196	1.10 (0.94–1.29)
Age			
<65 yr	421	457	0.99 (0.83–1.18)
≥65 yr	504	468	1.04 (0.94–1.15)
Time to ROSC from cardiac arrest			
<25 min	419	416	1.09 (0.91–1.33)
≥25 min	506	509	1.02 (0.92–1.12)
Initial rhythm			
Nonshockable	259	231	1.04 (0.94–1.14)
Shockable	666	694	1.00 (0.87–1.15)
Shock on admission			
Not present	665	651	1.07 (0.95–1.23)
Present	260	274	1.01 (0.89–1.15)

TTM2


A Death at 6 Months
Subgroup
Hypothermia
Normothermia
no. of patients
Relative Risk of Death (95% CI)
All patients 925 925 1.04 (0.94–1.14)
Sex
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Female 187 196 1.10 (0.94–1.29)
Age
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Time to ROSC from cardiac arrest
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Initial rhythm
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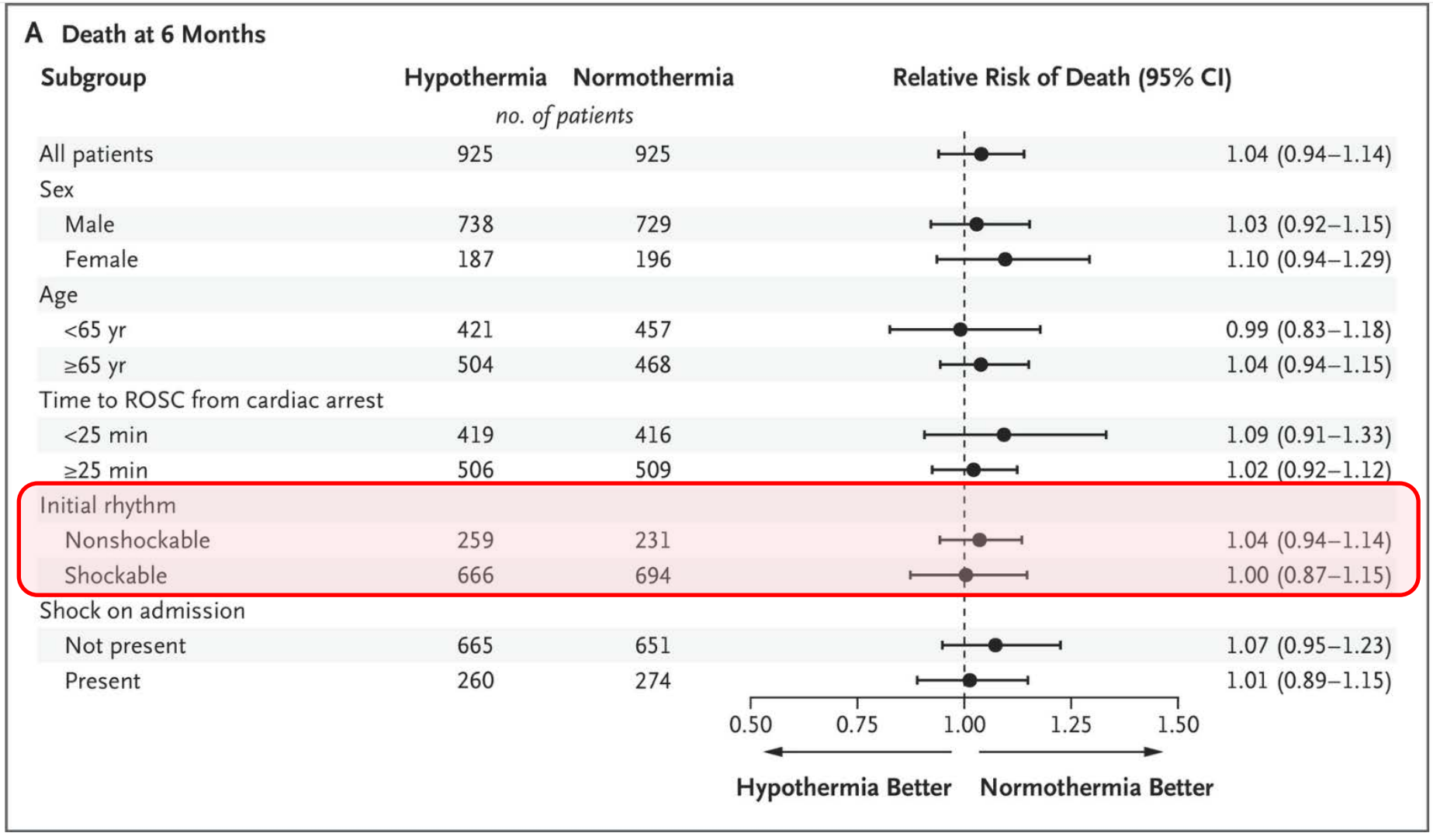
Shockable 666 694 1.00 (0.87–1.15)
Shock on admission
Not present 665 651 1.07 (0.95–1.23)
Present 260 274 1.01 (0.89–1.15)
0.50
0.75
1.00
1.25
1.50
Hypothermia Better
Normothermia Better

TTM2



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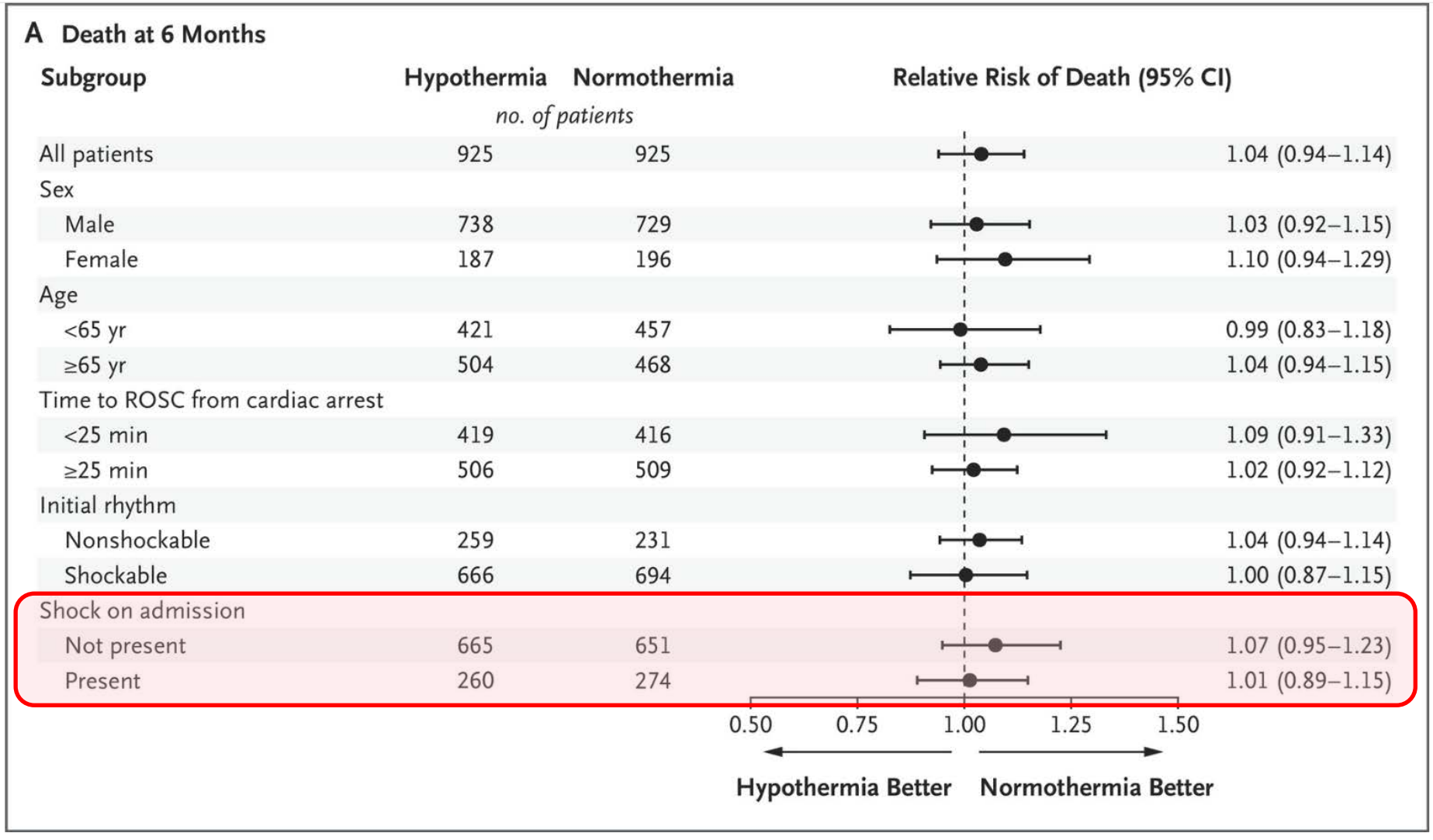
TTM2



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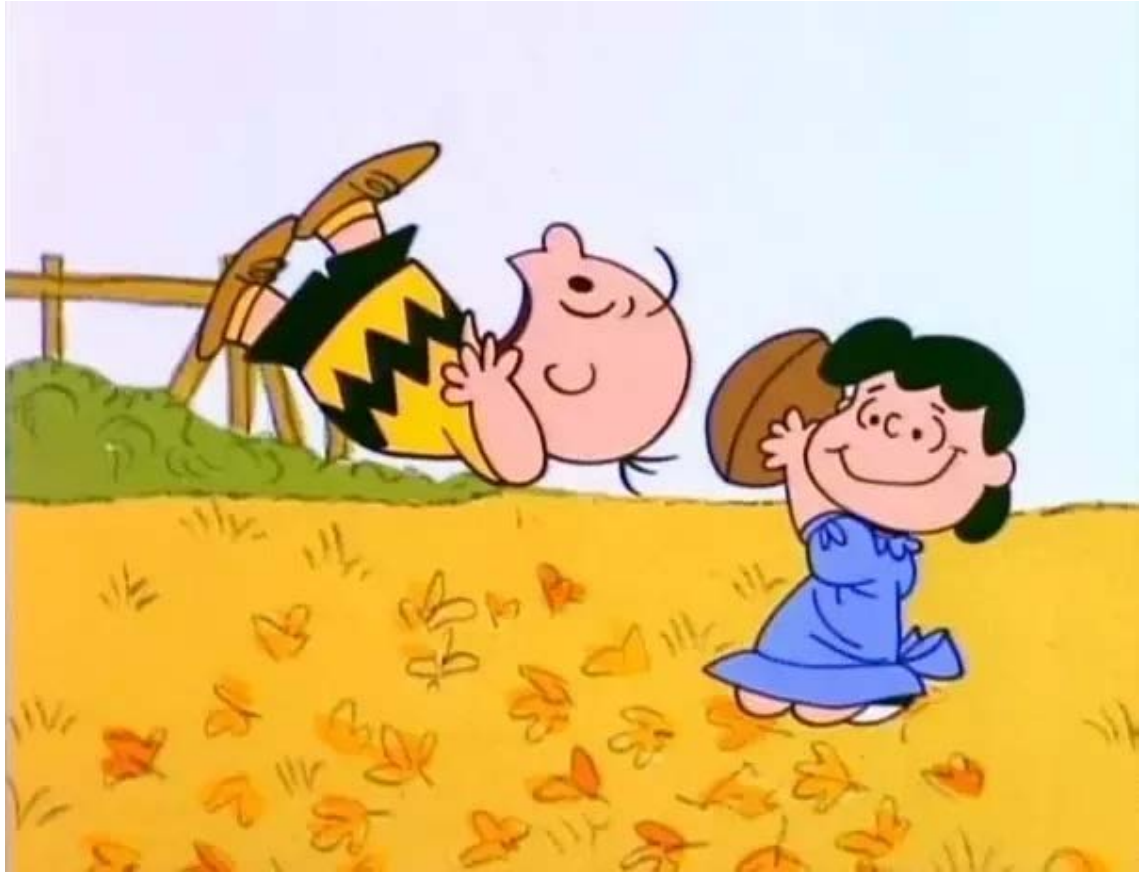
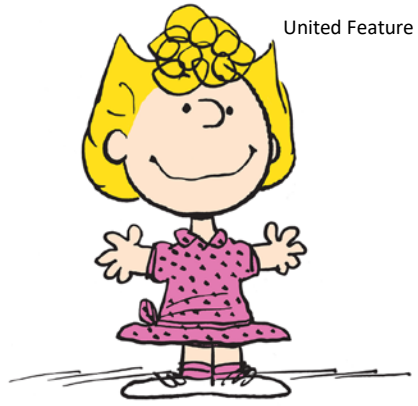
Going forward



United Feature Syndicate

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



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

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

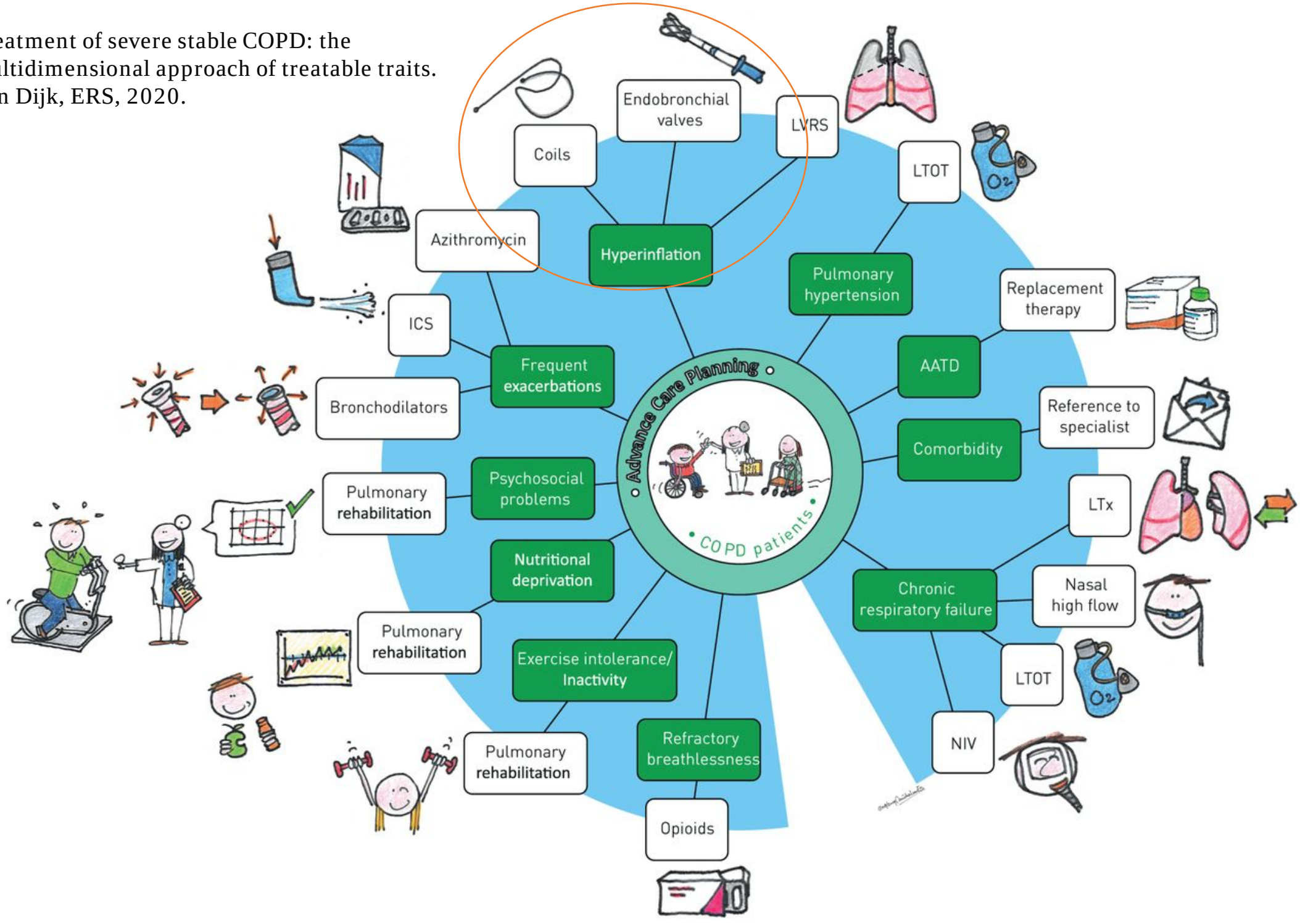
- The counterargument to continue cooling:
  - HYPERION (survival 18%) fits our population better than TTM2 (survival 51%)
  - Awaiting ICECAP results
    - ICECAP: Influence of Cooling Duration on Efficacy in Cardiac Arrest Patients
    - Cool withing 4 hours, duration 6-72 hours

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?”

https://www.everydayhealth.com/copd/guide/complications/

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

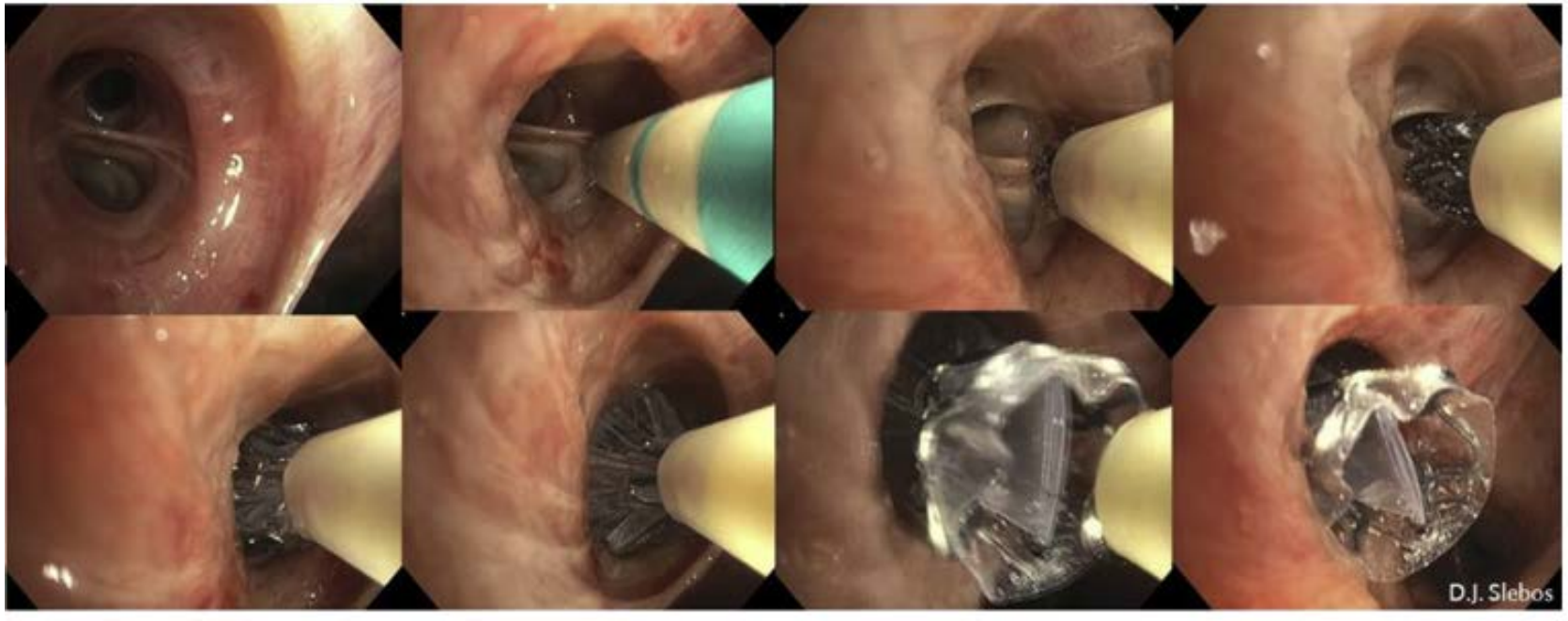


CHEST

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

The NEW ENGLAND JOURNAL of MEDICINE

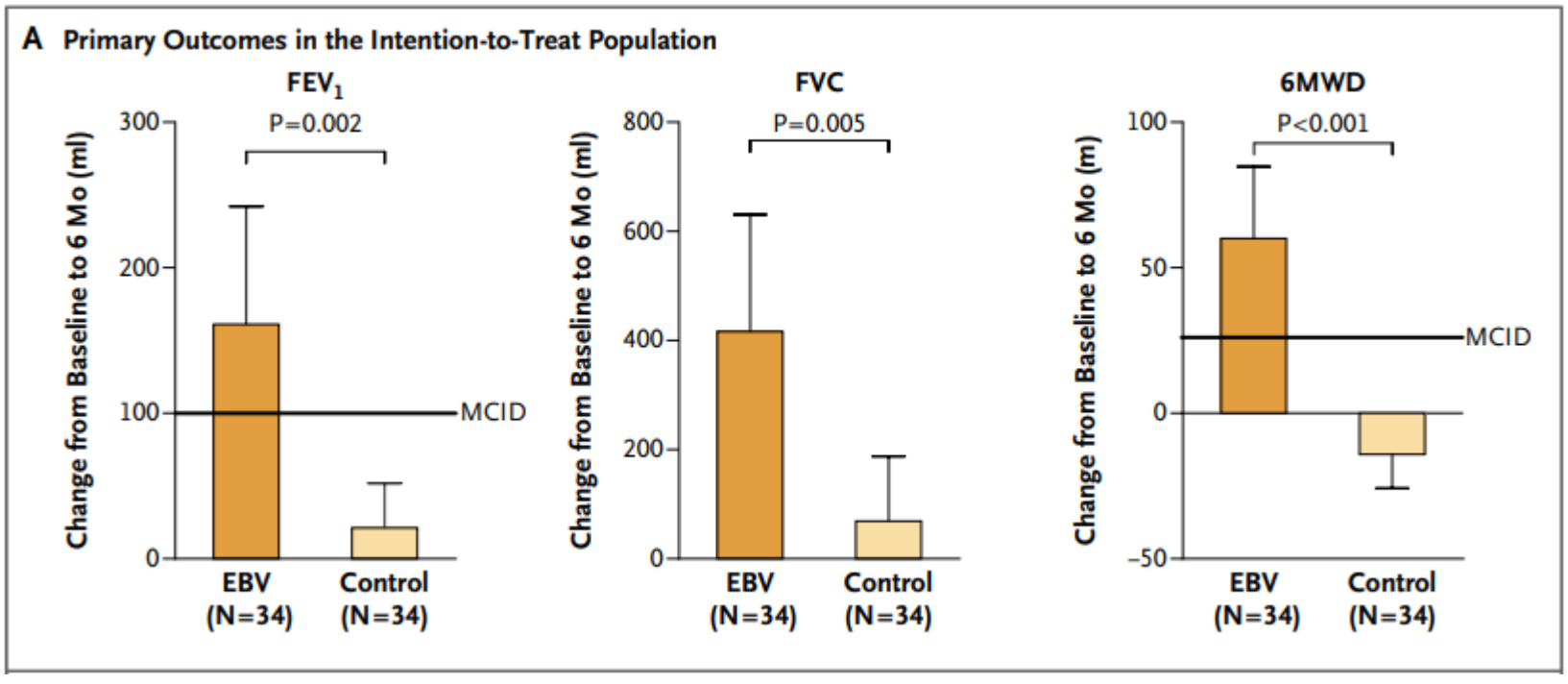
2015, NEJM

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



CHEST

Endobronchial Valves for the Treatment of

Check for updates

A. Heterogenous emphysema, lower lobe predominant

[COPD How I Do It]

CHEST

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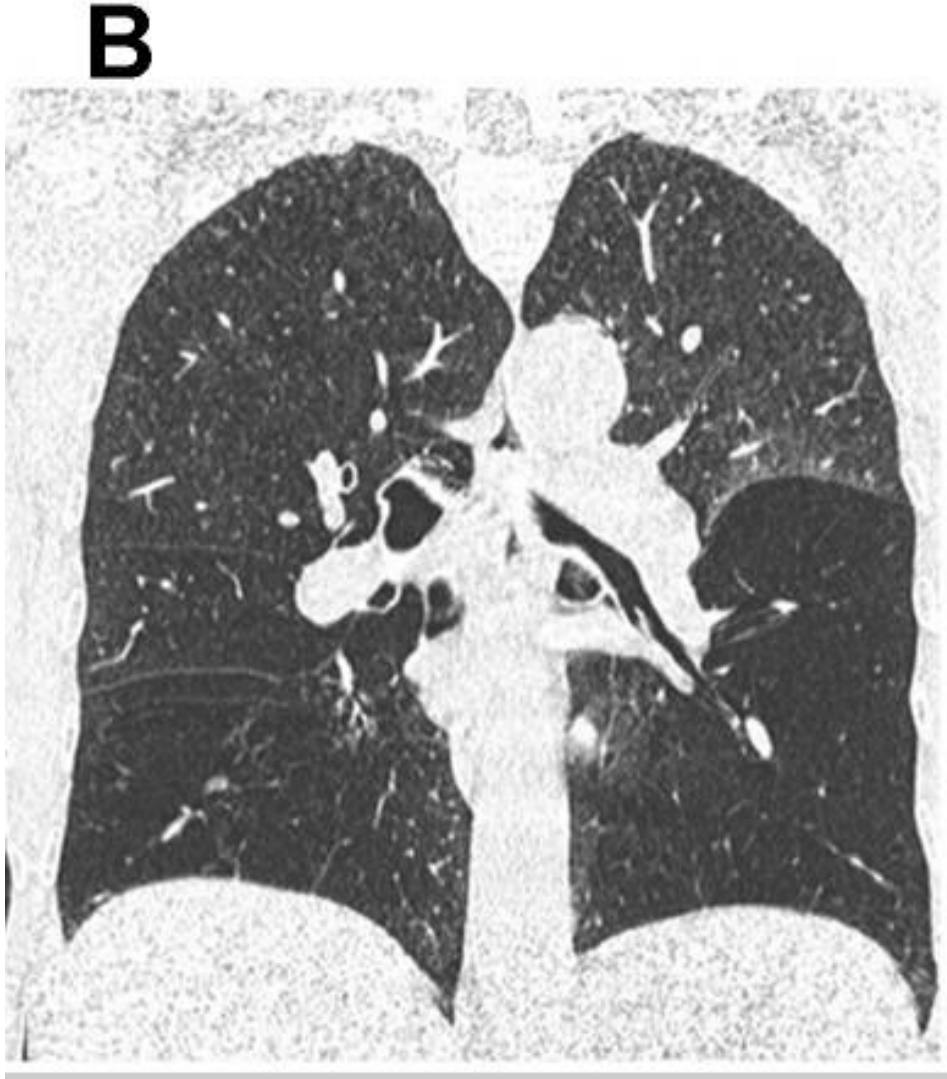

A. Heterogenous emphysema, lower lobe predominant
B. Expiration phase, air trapping in LLL

[COPD How I Do It]

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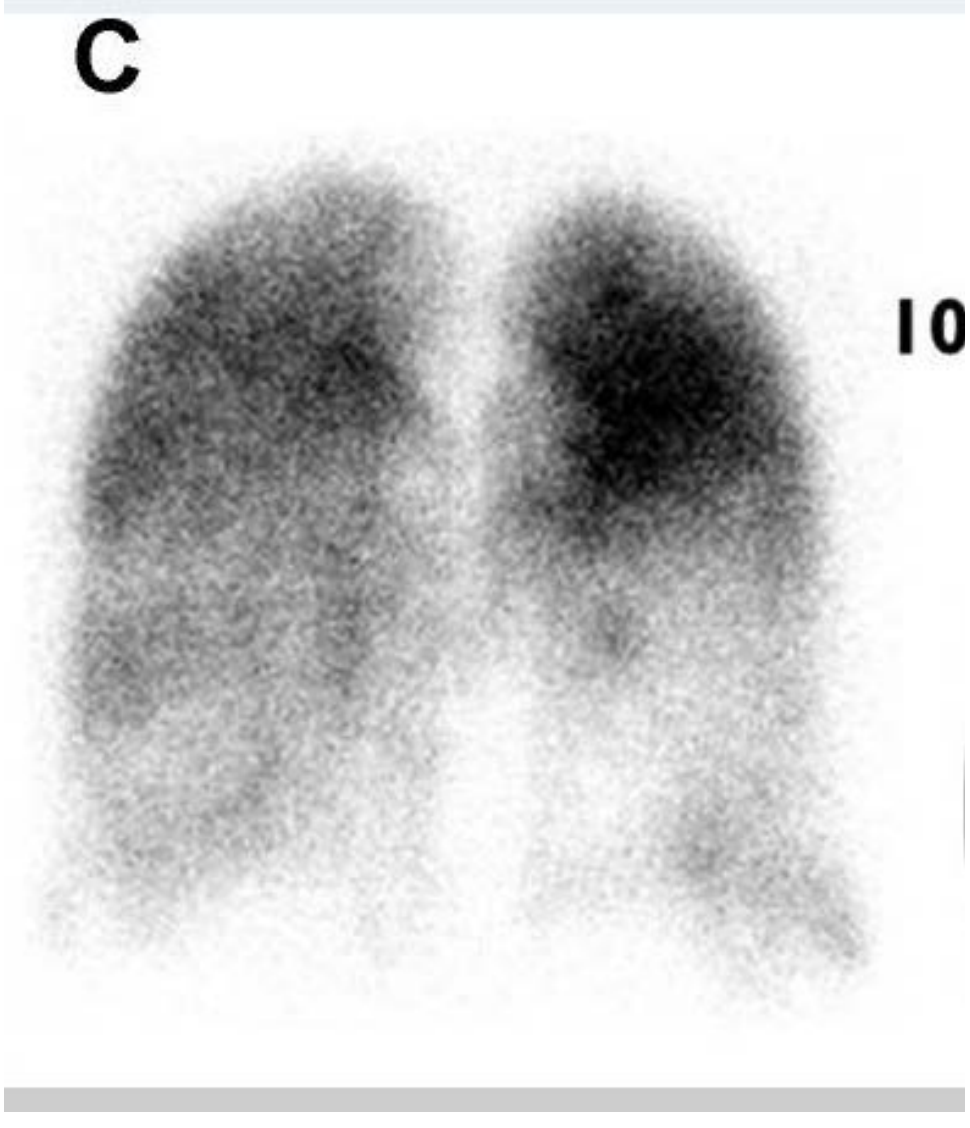

A. Heterogenous emphysema, lower lobe predominant
B. Expiration phase, air trapping in LLL
C. Perfusion scan shows absence of LLL perfusion

[COPD How I Do It]

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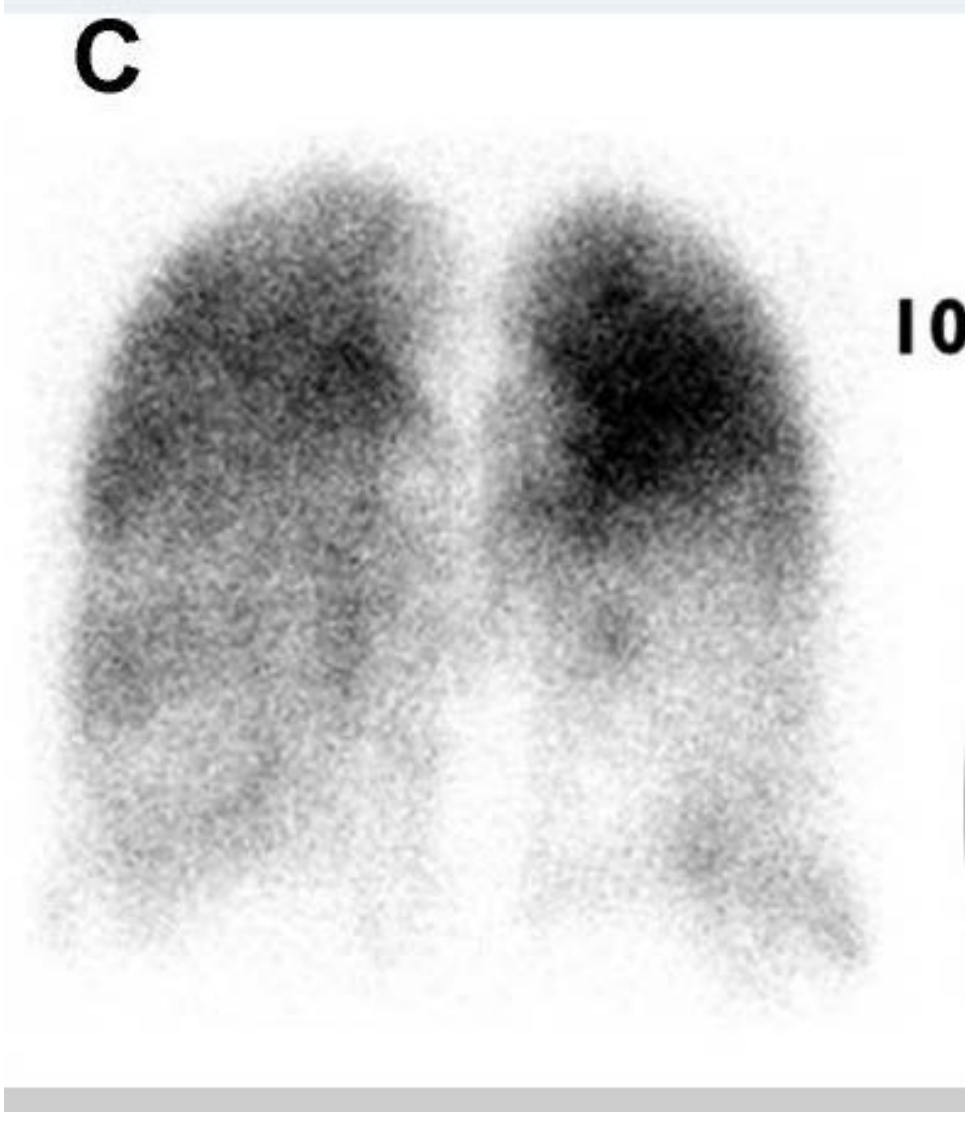

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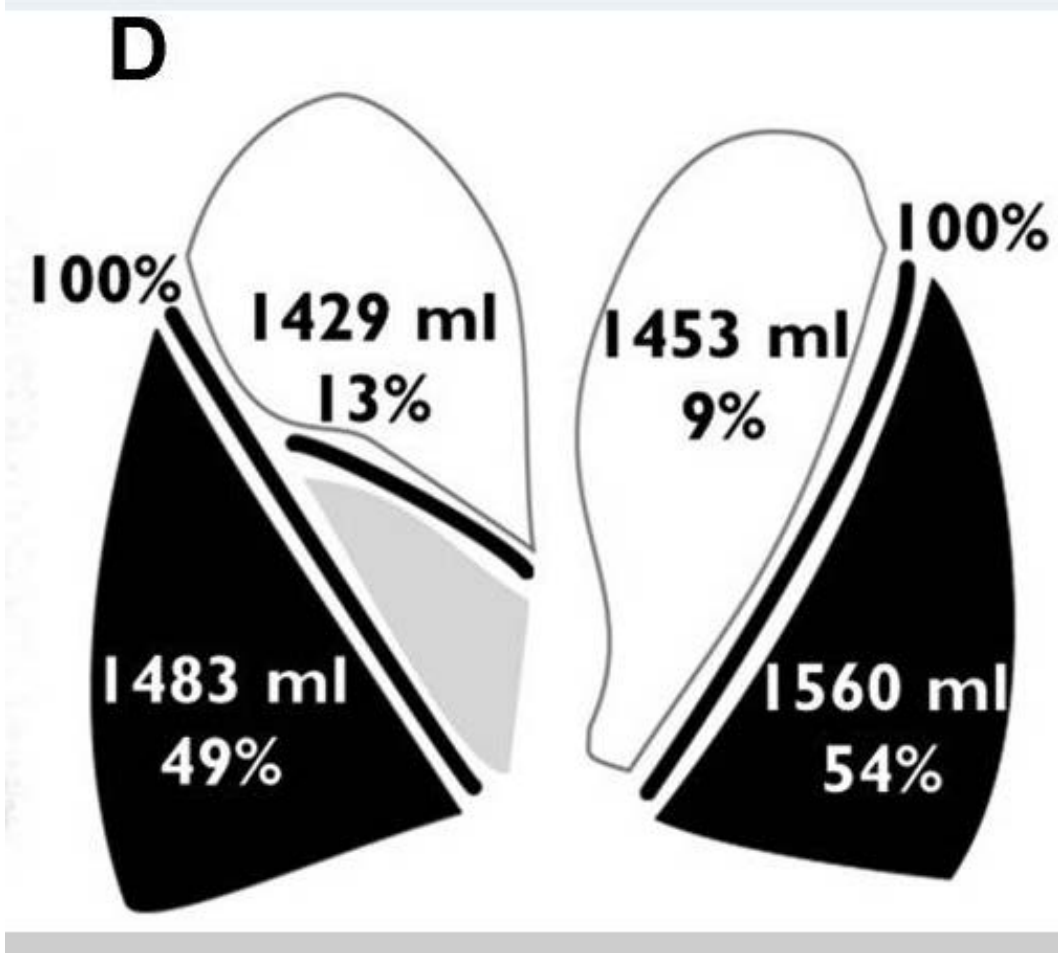
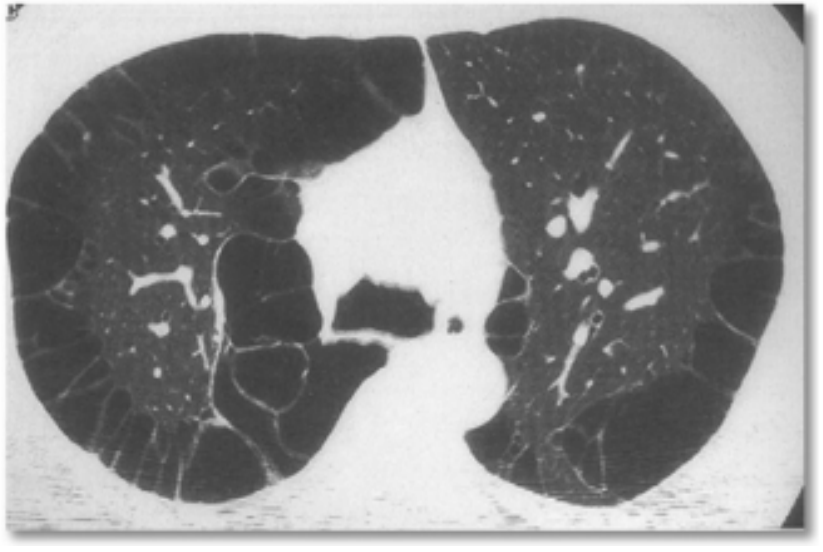


A. Heterogenous emphysema, lower lobe predominant
B. Expiration phase, air trapping in LLL
C. Perfusion scan shows absence of LLL perfusion
D. Quantitative CT scan shows
    A. emphysema in LLL (and RLL)
    B. Substantial lobar volume of LLL
    C. Fissure integrity

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 …"

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 1st 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. Lactated Ringers (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*

VANDERBILT UNIVERSITY

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

No benefit

Subgroup	Balanced Crystalloids	Saline	Odds Ratio (95% CI)	P Value	P Value for Interaction
	no. of events/total no. (%)				
Unit					0.27
Medical	615/2735 (22.5)	659/2646 (24.9)	0.87 (0.77–0.99)	0.04	
Cardiac	202/1470 (13.7)	190/1501 (12.7)	1.10 (0.89–1.36)	0.38	
Neurologic	116/1440 (8.1)	141/1377 (10.2)	0.77 (0.59–0.99)	0.04	
Trauma	131/1640 (8.0)	142/1688 (8.4)	0.95 (0.74–1.21)	0.66	
Surgical	75/657 (11.4)	79/648 (12.2)	0.93 (0.66–1.30)	0.66	
Sepsis					0.06
No	744/6775 (11.0)	756/6691 (11.3)	0.96 (0.86–1.07)	0.47	
Yes	395/1167 (33.8)	455/1169 (38.9)	0.80 (0.67–0.94)	0.01	
Traumatic brain injury					0.24
No	1034/7244 (14.3)	1118/7195 (15.5)	0.89 (0.81–0.98)	0.01	
Yes	105/698 (15.0)	93/665 (14.0)	1.09 (0.81–1.47)	0.58	
Categories of kidney function					0.19
Normal	476/5596 (8.5)	514/5561 (9.2)	0.91 (0.80–1.04)	0.16	
Acute kidney injury	315/574 (54.9)	316/537 (58.8)	0.85 (0.67–1.08)	0.18	
Chronic kidney disease	301/1388 (21.7)	307/1360 (22.6)	0.95 (0.79–1.13)	0.55	
Previous renal-replacement therapy	47/384 (12.2)	74/402 (18.4)	0.61 (0.41–0.91)	0.01	
Overall	1139/7942 (14.3)	1211/7860 (15.4)	0.91 (0.83–0.99)	0.04	

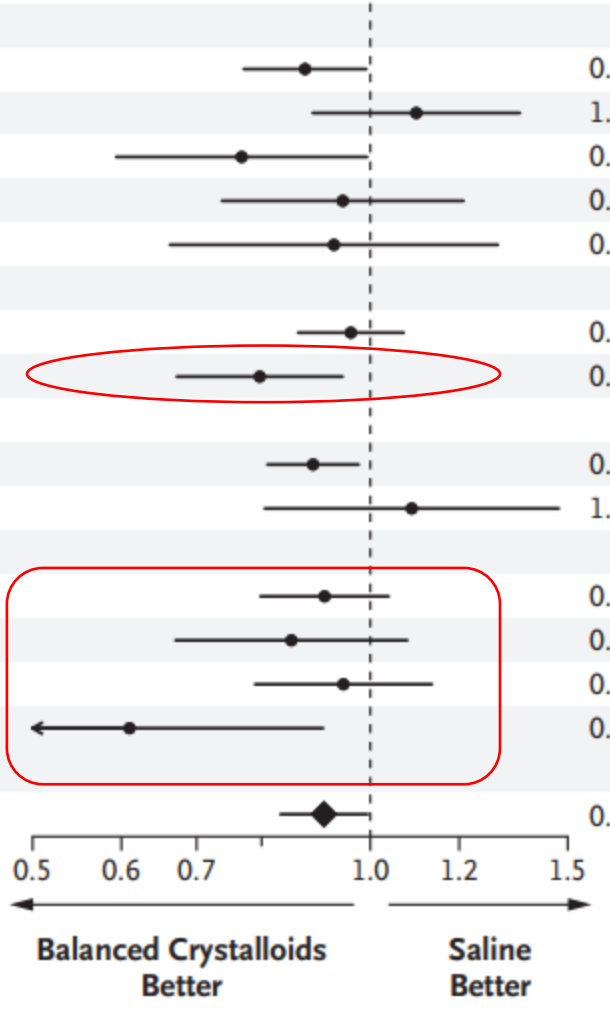


Figure 3. Subgroup Analysis of Rates for the Composite Outcome of Death, New Receipt of Renal-Replacement Therapy, or Persistent Renal Dysfunction.

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

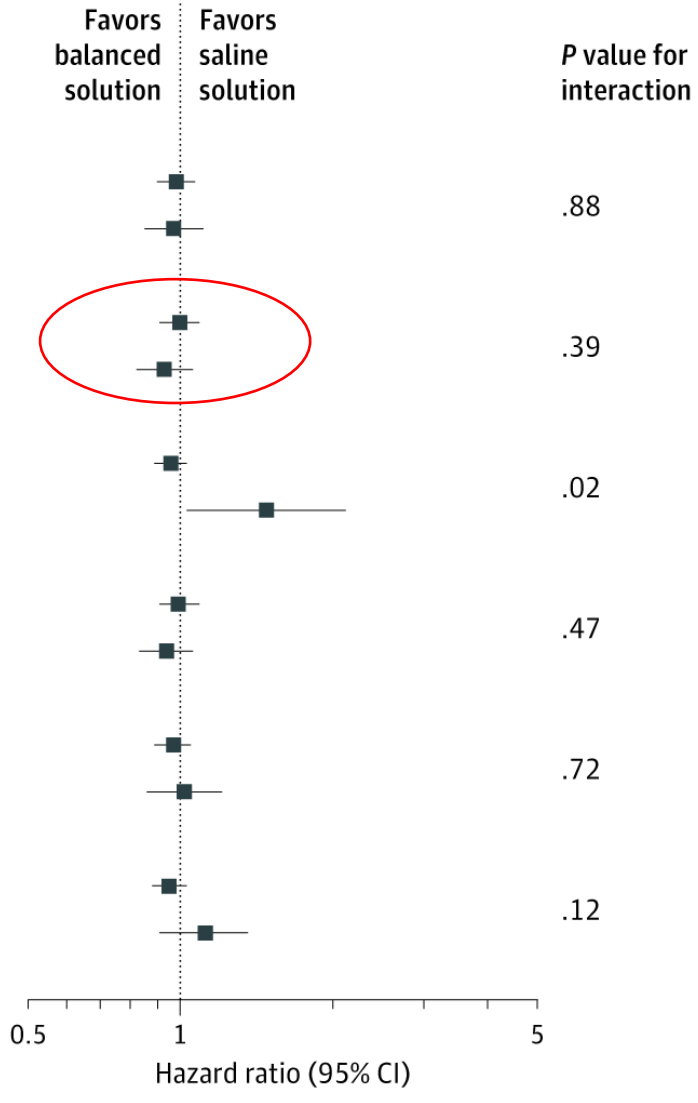
» Author Affiliations | Article Information

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

Subgroup	No. for 90-d mortality/total (%)[a]		Hazard ratio (95% CI)	*P* value for interaction
	Balanced solution	Saline solution[b]		
KDIGO stage for acute kidney injury[c]				
<2	989/4360 (22.7)	995/4350 (22.9)	0.98 (0.90-1.07)	.88
≥2	392/870 (45.1)	444/940 (47.2)	0.97 (0.85-1.11)	
Sepsis				
No	928/4260 (21.8)	941/4273 (22.0)	1.00 (0.91-1.09)	.39
Yes	453/970 (46.7)	498/1017 (49.0)	0.93 (0.82-1.06)	
Traumatic brain injury				
No	1303/4981 (26.2)	1389/5053 (27.5)	0.96 (0.89-1.03)	.02
Yes	78/249 (31.3)	50/237 (21.1)	1.48 (1.03-2.12)	
Surgical patients				
No	880/2078 (42.3)	891/2046 (43.5)	0.99 (0.91-1.09)	.47
Yes	501/3152 (15.9)	548/3244 (16.9)	0.94 (0.83-1.06)	
APACHE II score[d]				
<25	1131/4865 (23.2)	1170/4886 (23.9)	0.97 (0.89-1.05)	.72
≥25	250/365 (68.5)	269/404 (66.6)	1.02 (0.86-1.21)	
Administration of saline solution 24 h before randomization, L				
<1.0	1181/4277 (27.6)	1229/4286 (28.7)	0.95 (0.88-1.03)	.12
≥1.0	193/935 (20.6)	203/994 (20.4)	1.12 (0.91-1.36)	



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 3, 2022 VOL. 386 NO. 9

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.

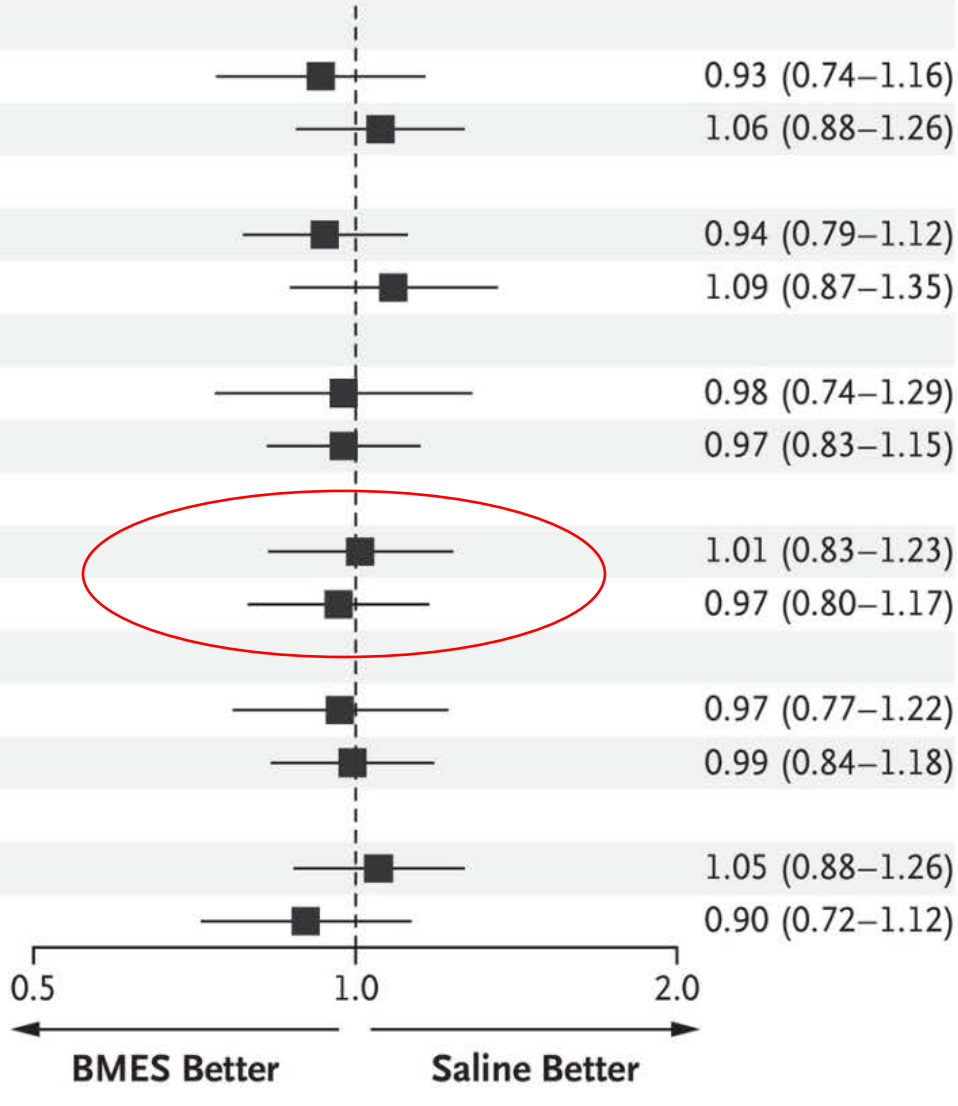
The authors' affiliations are listed in the Appendix. Dr. Finfer can be contacted at sfinfer@georgeinstitute.org.au or at the George Institute for Global Health, 1 King

90 day mortality

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

B Subgroup Analysis of Death from Any Cause

Subgroup	BMES Group	Saline Group	Odds Ratio (95% CI)
	no. of events/total no. (%)		
Age			
<65 yr	184/1250 (14.7)	188/1207 (15.6)	0.93 (0.74–1.16)
≥65 yr	346/1183 (29.2)	342/1206 (28.4)	1.06 (0.88–1.26)
Sex			
Male	328/1531 (21.4)	323/1437 (22.5)	0.94 (0.79–1.12)
Female	202/902 (22.4)	207/976 (21.2)	1.09 (0.87–1.35)
Kidney injury			
Yes	160/468 (34.2)	155/451 (34.4)	0.98 (0.74–1.29)
No	361/1934 (18.7)	370/1931 (19.2)	0.97 (0.83–1.15)
Sepsis			
Yes	276/1068 (25.8)	265/1026 (25.8)	1.01 (0.83–1.23)
No	254/1362 (18.6)	265/1386 (19.1)	0.97 (0.80–1.17)
Admitted from surgery			
Yes	171/1087 (15.7)	179/1109 (16.1)	0.97 (0.77–1.22)
No	359/1344 (26.7)	351/1304 (26.9)	0.99 (0.84–1.18)
APACHE II score			
<25	287/1753 (16.4)	275/1739 (15.8)	1.05 (0.88–1.26)
≥25	243/678 (35.8)	255/673 (37.9)	0.90 (0.72–1.12)



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

NEJM Evidence

Published January 18, 2022
NEJM Evid 2022; 1 (2)
DOI: 10.1056/EVIDoa2100010

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

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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*

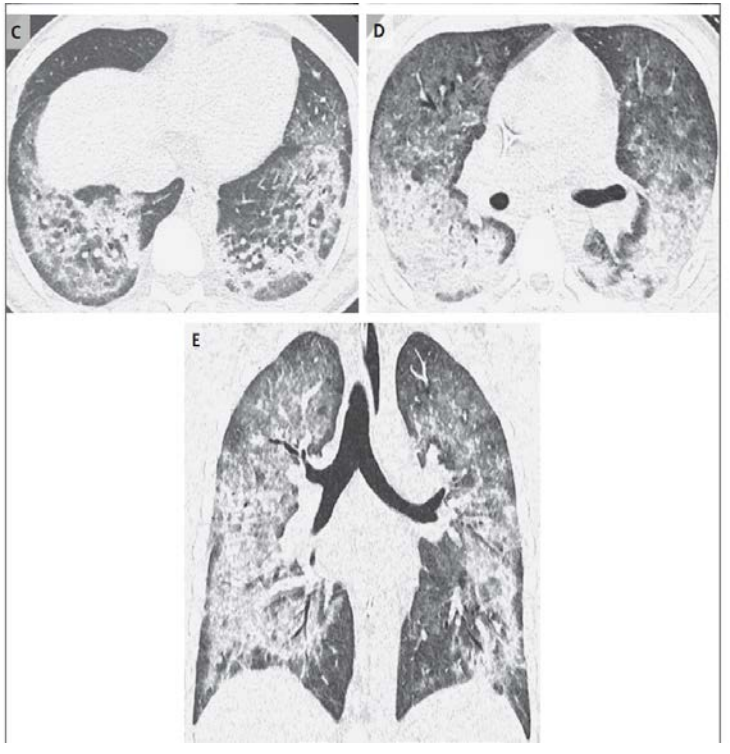
ABSTRACT

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 vaper → 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

End Point, According to Subgroup	Placebo (N=107)	Dupilumab (N=103)	Odds Ratio (95% CI)	Overall P Value for Interaction
	no. of patients			
Reduction of ≥50% in glucocorticoid dose				
≥300 or <300 cells/mm³				0.30
≥300	41	48	6.59 (2.13 to 20.42)	
<300	66	55	2.91 (1.28 to 6.63)	
≥150 or <150 cells/mm³				0.49
≥150	69	81	4.49 (2.04 to 9.85)	
<150	38	22	3.33 (0.97 to 11.48)	
Reduction of glucocorticoid dose to <5 mg/day				
≥300 or <300 cells/mm³				0.23
≥300	41	48	8.04 (2.71 to 23.82)	
<300	66	55	3.12 (1.41 to 6.93)	
≥150 or <150 cells/mm³				0.83
≥150	69	81	4.29 (2.04 to 9.04)	
<150	38	22	6.03 (1.70 to 21.44)	
Elimination of glucocorticoid use				
≥300 or <300 cells/mm³				0.41
≥300	40	48	4.07 (1.46 to 11.33)	
<300	66	55	2.15 (0.96 to 4.81)	
≥150 or <150 cells/mm³				0.97
≥150	68	81	2.73 (1.31 to 5.70)	
<150	38	22	3.15 (0.93 to 10.73)	

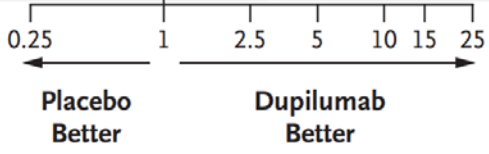
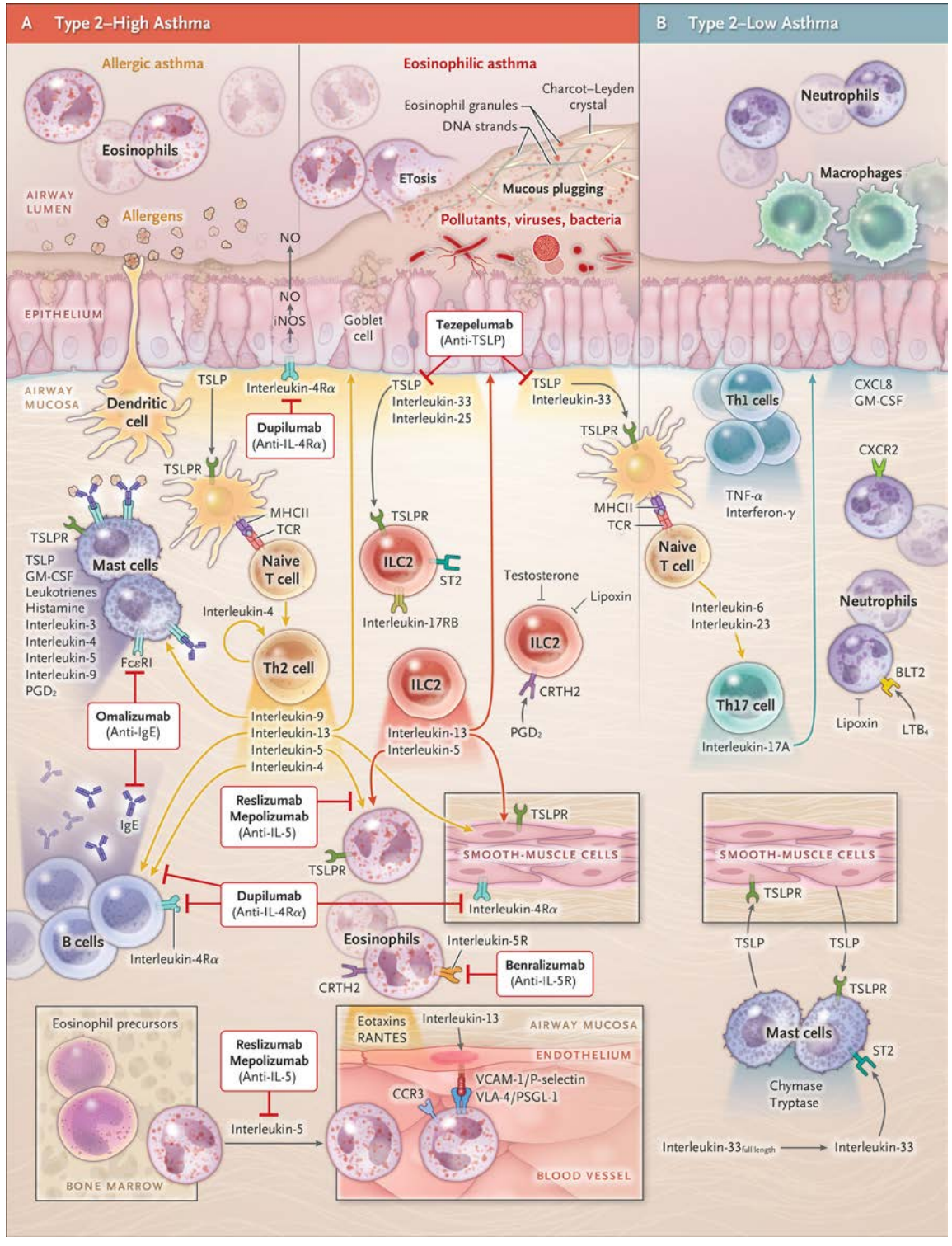


Figure 2. Primary End Point and Secondary Oral Glucocorticoid End Points at Week 24, According to Baseline Blood Eosinophil Subgroup.

Rabe, et al, NEJM, 2018, for Dupixent


A Type 2–High Asthma
B Type 2–Low Asthma
Allergic asthma
Eosinophilic asthma
Eosinophil granules
Charcot–Leyden crystal
DNA strands
Eosinophils
ETosis
Mucous plugging
AIRWAY LUMEN
Allergens
Pollutants, viruses, bacteria
Neutrophils
Macrophages
NO
NO
iNOS
EPITHELIUM
Goblet cell
Tezepelumab (Anti-TSLP)
AIRWAY MUCOSA
Dendritic cell
TSLP
Interleukin-4Rα
Dupilumab (Anti-IL-4Rα)
TSLP
Interleukin-33
Interleukin-25
TSLP
Interleukin-33
Th1 cells
CXCL8
GM-CSF
TSLPR
TSLPR
MHCII
TCR
Naive T cell
TSLPR
ILC2
ST2
Interleukin-17RB
MHCII
TCR
Naive T cell
TNF-α
Interferon-γ
CXCR2
TSLPR
Mast cells
TSLP
GM-CSF
Leukotrienes
Histamine
Interleukin-3
Interleukin-4
Interleukin-5
Interleukin-9
PGD2
Interleukin-4
Th2 cell
FcεRI
Testosterone
Lipoxin
ILC2
CRTH2
PGD2
Interleukin-6
Interleukin-23
Neutrophils
BLT2
Lipoxin
LTB4
Th17 cell
Interleukin-17A
Omalizumab (Anti-IgE)
Interleukin-9
Interleukin-13
Interleukin-5
Interleukin-4
ILC2
Interleukin-13
Interleukin-5
IgE
Reslizumab Mepolizumab (Anti-IL-5)
TSLPR
SMOOTH-MUSCLE CELLS
TSLPR
Interleukin-4Rα
SMOOTH-MUSCLE CELLS
TSLPR
Dupilumab (Anti-IL-4Rα)
B cells
Interleukin-4Rα
Eosinophils
Interleukin-5R
CRTH2
Benralizumab (Anti-IL-5R)
TSLP
TSLP
TSLPR
Mast cells
ST2
Chymase
Tryptase
Interleukin-33full length
Interleukin-33
Eosinophil precursors
BONE MARROW
Reslizumab Mepolizumab (Anti-IL-5)
Interleukin-5
Eotaxins
RANTES
Interleukin-13
AIRWAY MUCOSA
ENDOTHELIUM
VCAM-1/P-selectin
VLA-4/PSGL-1
CCR3
BLOOD VESSEL

Your shift is over

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, <u>in the right patient.</u>

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?

WE ARE Valley

Acknowledgements

- Deepthi Mani
- ACP WA leadership

- richard_kim@valleymed.org

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