

대한 결핵 및 호흡기 학회
제 46 차 Workshop

Respiratory Review of 2018

Critical Care Medicine

허진원

울산의대 서울아산병원



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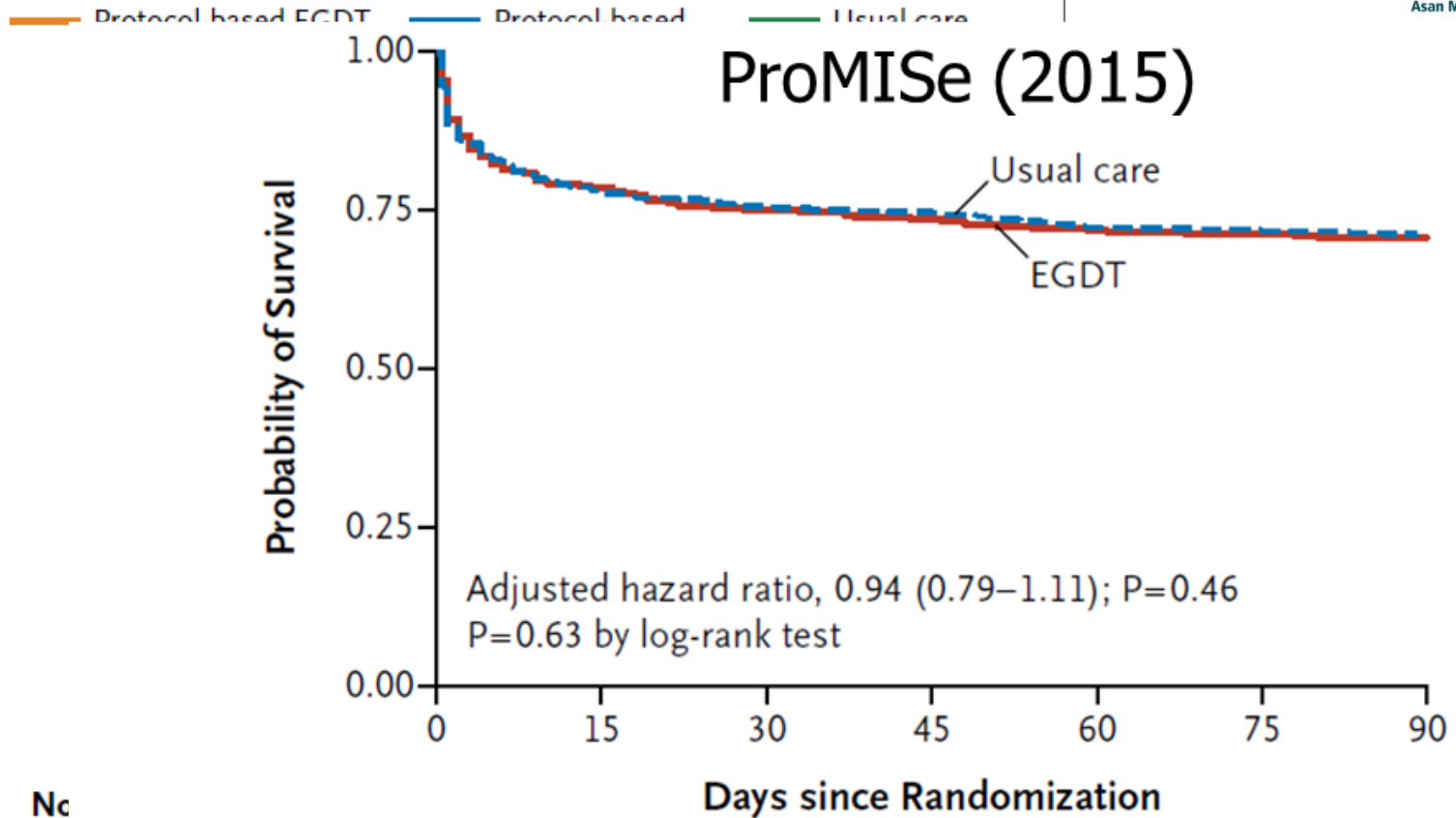
02. Respiratory Care

03. Nutrition

04. Delirium



1. SEPSIS



Ac
Pr
≥65 a

	No. a	Nc	No. at Risk						
	Protol	EGDT							
	Usual care	Usual care	0	15	30	45	60	75	90
Protol	625	EGDT	625	492	470	461	449	445	440
Usual care	626	Usual care	626	487	469	464	448	445	439

Rivers et al. N Engl J Med 2001;345:1368-77

Early, Goal-Directed Therapy for Septic Shock — A Patient-Level Meta-Analysis



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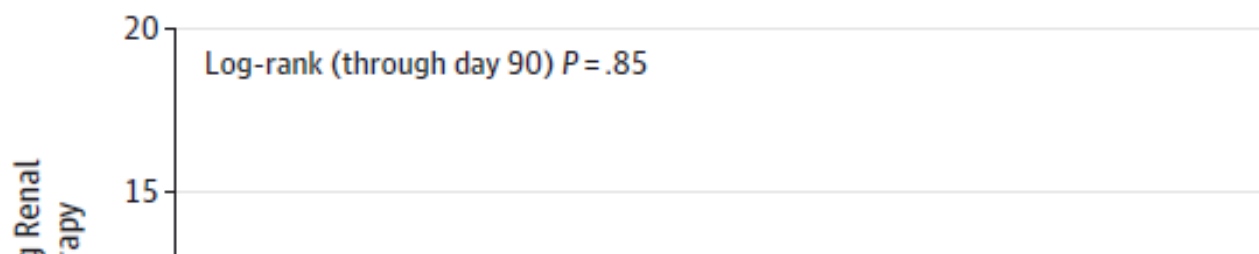
Outcome	EGDT (N=1857)	Usual Care (N=1880)	Incremental Effect (95% CI)	P Value	
				Overall Comparison	Comparison among Trials
Primary outcome: death at 90 days — no./total no. (%)	462/1852 (24.9)	475/1871 (25.4)	0.97 (0.82 to 1.14) ^{†‡}	0.68	0.73
Secondary outcomes: mortality					
Death at hospital discharge — no./total no. (%) [§]	370/1857 (19.9)	365/1878 (19.4)	1.02 (0.85 to 1.21) [†]	0.86	0.42
Death at 28 days — no./total no. (%)	375/1854 (20.2)	385/1873 (20.6)	0.96 (0.81 to 1.15) [†]	0.68	0.57
In ICU					
Admitted to ICU — no. (%)	1684 (90.7)	1532 (81.5)			
First stay — days					
Median among patients admitted	3	4			
IQR	2 to 6	2 to 6			
Mean overall	4.9±6.6	4.5±6.4	0.5 (0.1 to 0.9) [¶]	0.02	0.76
Total stay, including readmissions — days					
Median among patients admitted	4	4			
IQR	2 to 7	2 to 7			
Mean overall	5.3±7.1	4.9±7.0	0.5 (0.0 to 0.9) [¶]	0.04	0.78
Cardiovascular support: vasopressors or inotropes in ICU					
Receipt — no./total no. (%)	1040/1854 (56.1)	923/1873 (49.3)	1.42 (1.23 to 1.64) [†]	<0.001	0.40
Duration — days					
Median among patients receiving support	2	2			
IQR	1 to 4	1 to 4			
Mean overall	1.9±3.7	1.6±2.9	0.3 (0.1 to 0.5) [¶]	0.01	0.52

Initial resuscitation

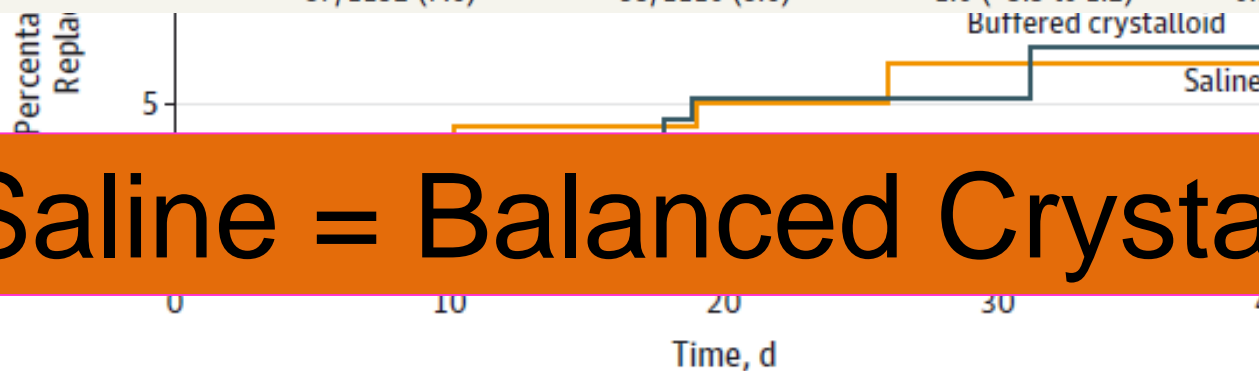
- sepsis-induced hypoperfusion : at least 30 mL/kg of IV crystalloid fluid within the first 3 hours
- We recommend **crystalloids** as the fluid of choice for initial resuscitation and subsequent intravascular volume replacement
- We suggest using either **balanced crystalloids or saline** for fluid resuscitation
- We suggest using **albumin** in addition to crystalloids for initial resuscitation and subsequent intravascular volume replacement
- We recommend **against using hydroxyethyl starches (HESs)**

Type of fluid

Effect of a Buffered Crystalloid Solution vs Saline on Acute Kidney Injury Among Patients in the Intensive Care Unit (SPLIT trial)



Mortality	Buffered Crystalloid	Saline	HR (95% CI)	OR (95% CI)	P
Death in ICU	76/1152 (6.6)	80/1110 (7.2)	-0.6 (-2.7 to 1.5)	0.92 (0.68 to 1.24)	.62
Death in hospital	87/1152 (7.6)	95/1110 (8.6)	-1.0 (-3.3 to 1.2)	0.88 (0.67 to 1.17)	.40



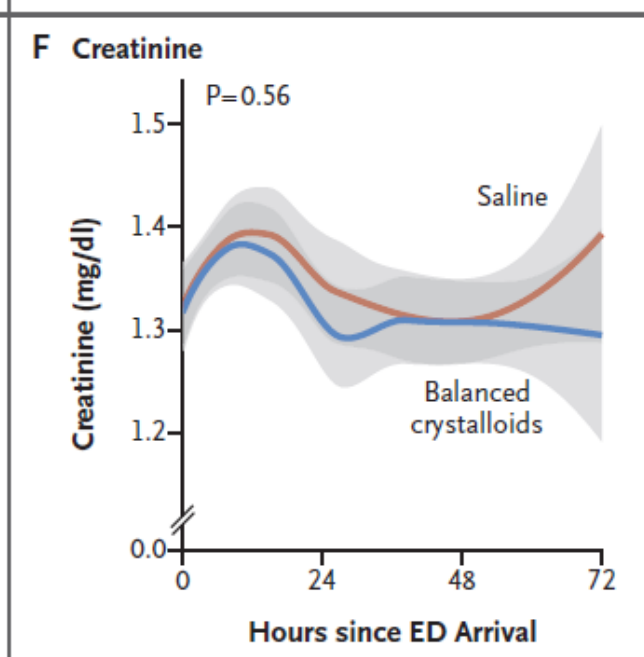
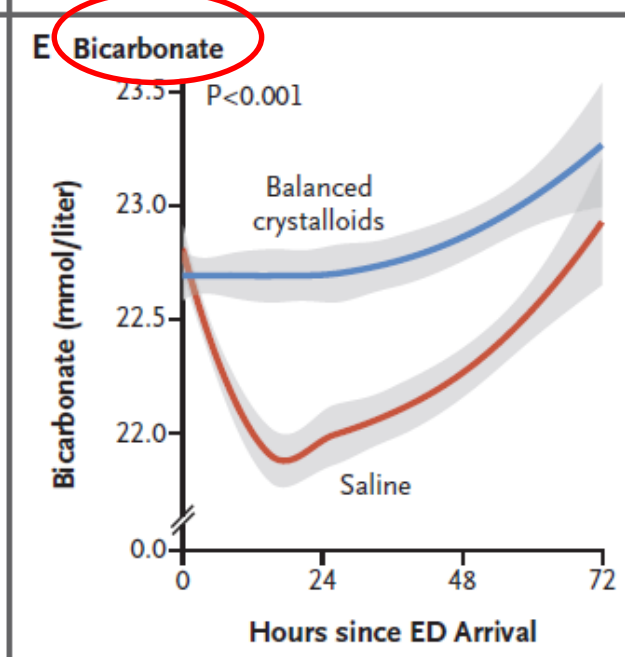
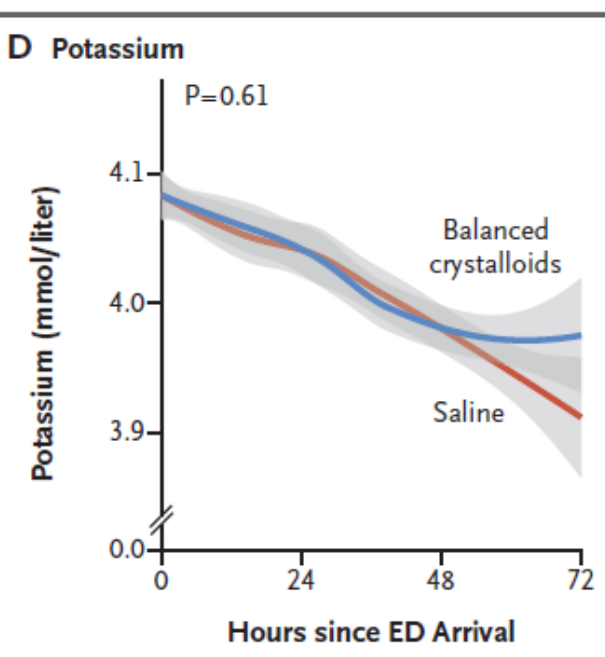
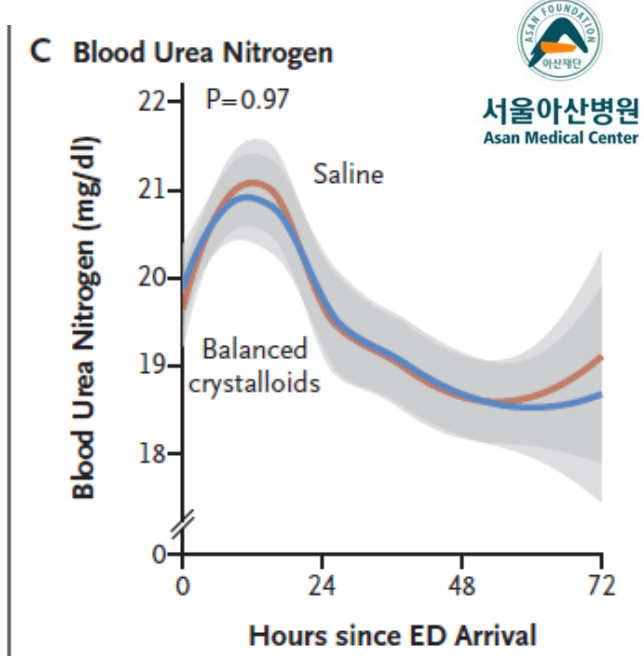
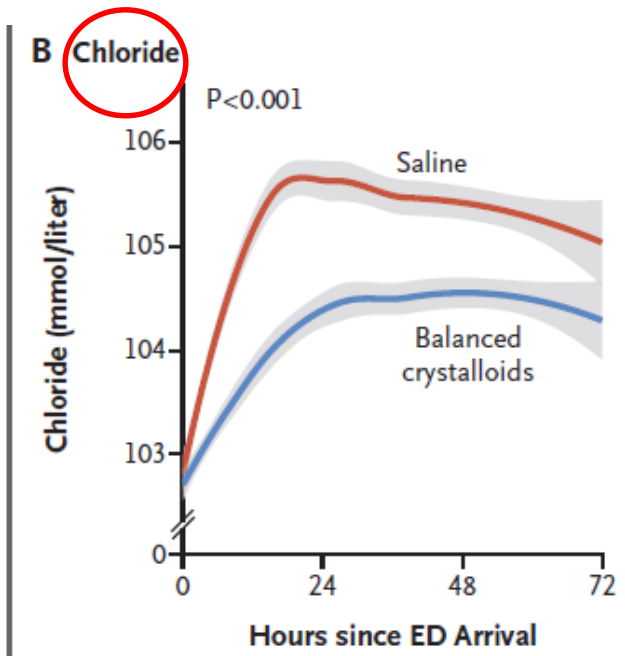
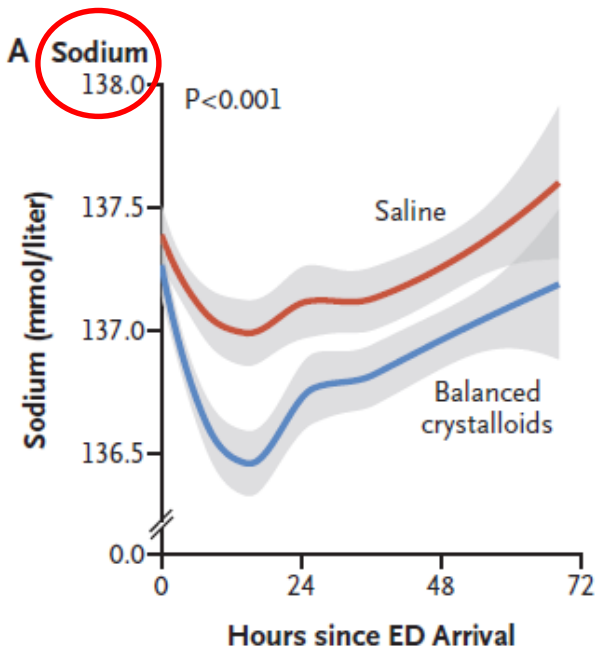
Saline = Buffered Crystalloid

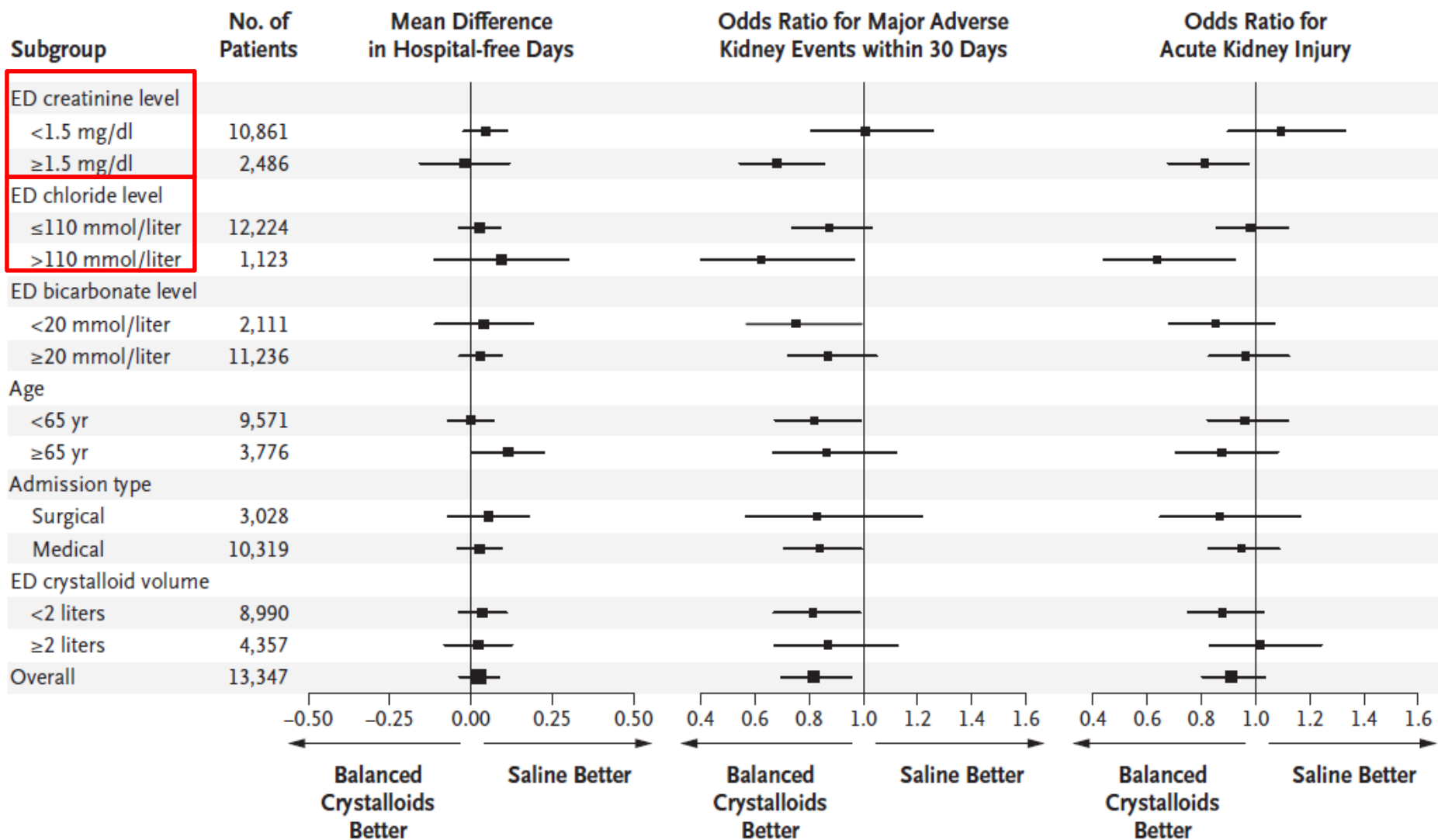
No. at risk	0	10	20	30	40
Buffered crystalloid	1152	341	134	62	36
Saline	1110	310	124	64	28

Balanced Crystalloids versus Saline in Noncritically Ill Adults (SALT-ED trial)

Table 3. Clinical Outcomes According to Assigned Treatment Group in the Intention-to-Treat Analysis.

Outcome	Balanced Crystalloids (N = 6708)	Saline (N = 6639)	Adjusted Odds Ratio (95% CI)*	Adjusted P Value
Median hospital-free days to day 28 (IQR)	25 (22–26)	25 (22–26)	0.98 (0.92–1.04)	0.41
Major adverse kidney event within 30 days — no. (%)	315 (4.7)	370 (5.6)	0.82 (0.70–0.95)	0.01
✓ Death — no. (%)	94 (1.4)	102 (1.5)	0.89	
✓ New renal-replacement therapy — no./total no. (%)†	18/6582 (0.3)	31/6530 (0.5)	0.56	
✓ Final serum creatinine ≥200% of baseline — no./total no. (%)†	253/6582 (3.8)	293/6530 (4.5)	0.84	
Stage 2 or higher acute kidney injury — no./total no. (%)†	528/6582 (8.0)	560/6530 (8.6)	0.91 (0.80–1.03)	0.14
In-hospital death — no. (%)	95 (1.4)	105 (1.6)	0.88 (0.66–1.16)	0.36

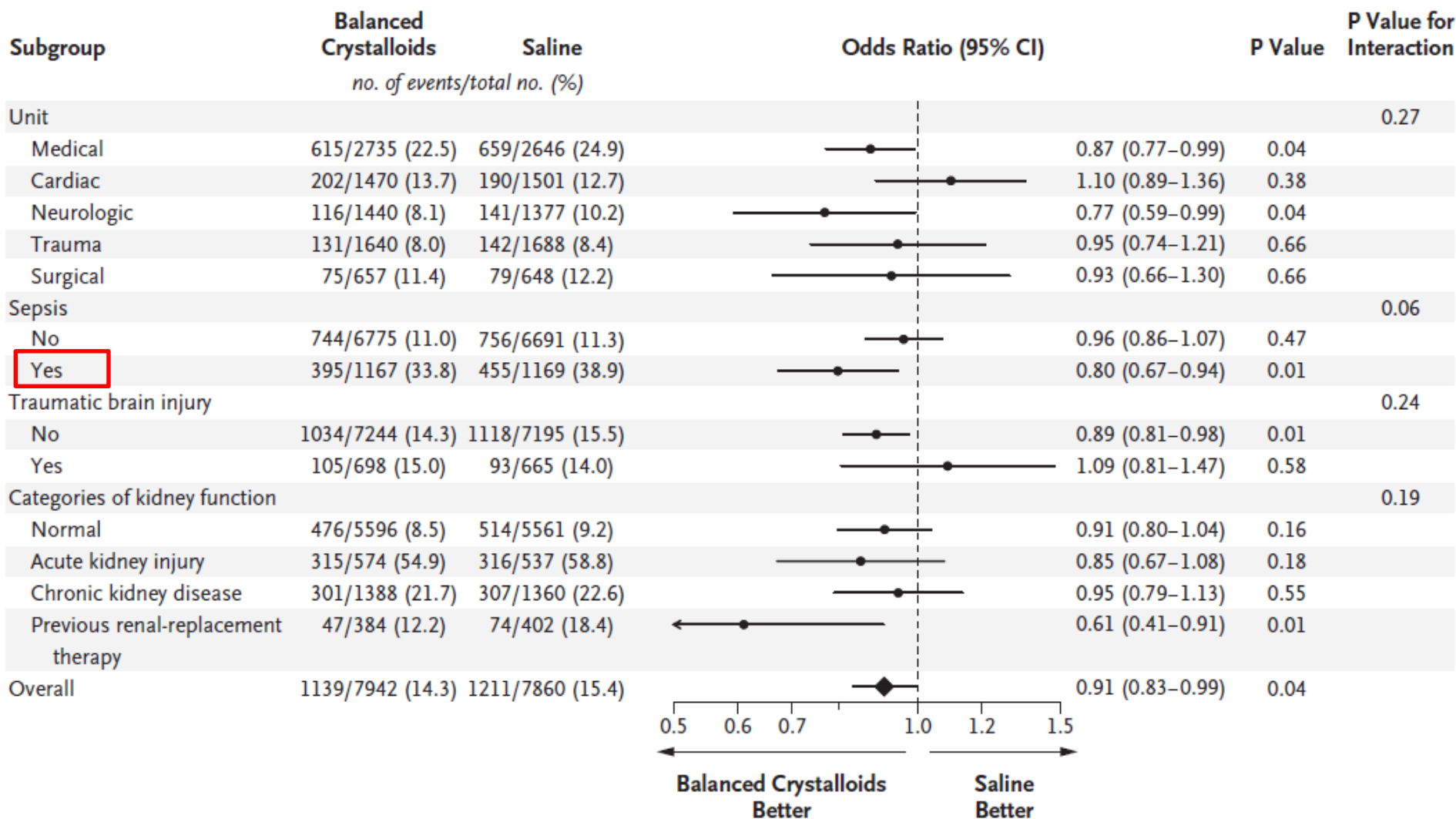




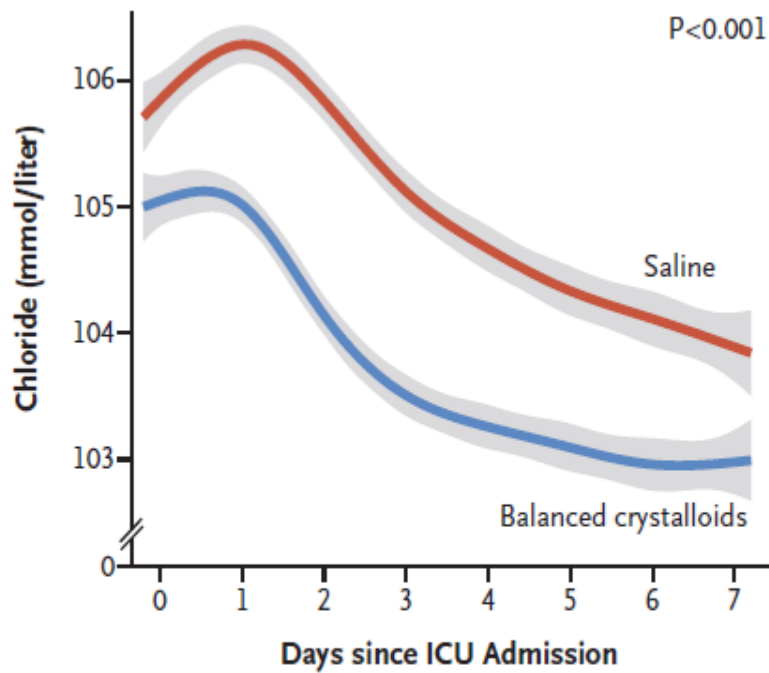
Balanced Crystalloids versus Saline in critically Ill Adults (SMART)



Outcome	Balanced Crystalloids (N=7942)	Saline (N=7860)	Adjusted Odds Ratio (95% CI) [†]	P Value [‡]
Primary outcome				
Major adverse kidney event within 30 days — no. (%) [‡]	1139 (14.3)	1211 (15.4)	0.90 (0.82 to 0.99)	0.04
Components of primary outcome				
In-hospital death before 30 days — no. (%)	818 (10.3)	875 (11.1)	0.90 (0.80 to 1.01)	0.06
Receipt of new renal-replacement therapy — no./total no. (%) [§]	189/7558 (2.5)	220/7458 (2.9)	0.84 (0.68 to 1.02)	0.08
Among survivors	106/6787 (1.6)	117/6657 (1.8)		
Final creatinine level ≥200% of baseline — no./total no. (%) [§]	487/7558 (6.4)	494/7458 (6.6)	0.96 (0.84 to 1.11)	0.60
Among survivors	259/6787 (3.8)	273/6657 (4.1)		
Among survivors without new renal-replacement therapy	215/6681 (3.2)	219/6540 (3.3)		
Secondary outcomes				
In-hospital death — no. (%)				
Before ICU discharge	528 (6.6)	572 (7.3)	0.89 (0.78 to 1.02)	0.08
Before 60 days	928 (11.7)	975 (12.4)	0.92 (0.83 to 1.02)	0.13
Renal-replacement therapy–free days [¶]			1.11 (1.02 to 1.20)	0.01
Median	28.0	28.0		
Interquartile range	28.0 to 28.0	28.0 to 28.0		
Mean	25.0±8.6	24.8±8.9		



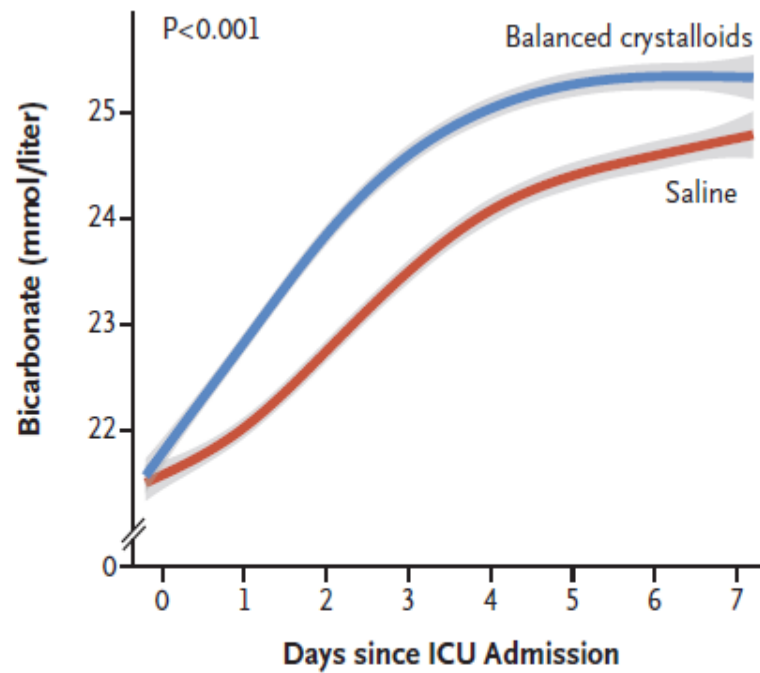
A Chloride Concentration



No. of Patients with Measurement

Balanced crystalloids	6904	4715	3263	2195
Saline	6747	4669	3283	2172

B Bicarbonate Concentration



No. of Patients with Measurement

Balanced crystalloids	6929	4718	3266	2198
Saline	6763	4678	3293	2175

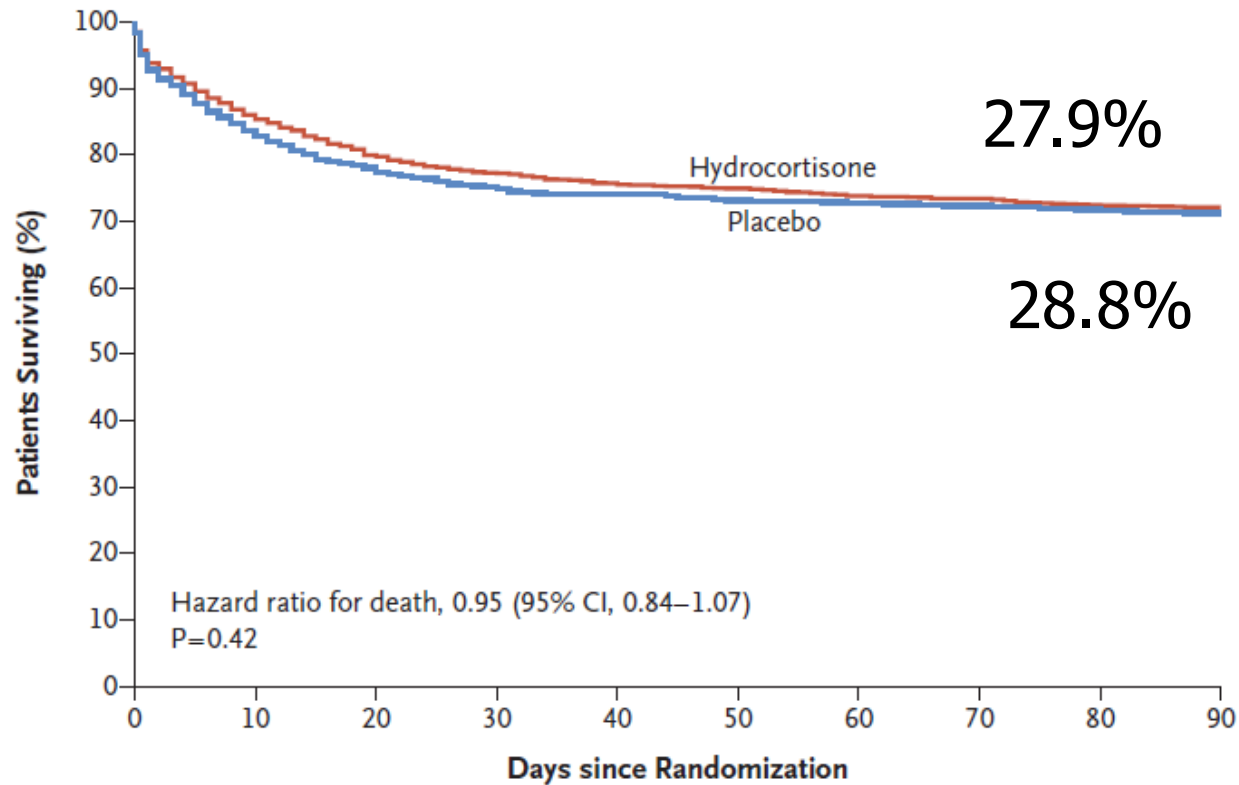
Steroid

We suggest **against** using IV hydrocortisone to treat septic shock patients if adequate fluid resuscitation and vasopressor therapy are able to restore hemodynamic stability. If this is not achievable, we suggest **IV hydrocortisone at a dose of 200 mg per day**

Hydrocortisone plus Fludrocortisone for Adults with Septic Shock (APROCCHSS trial)

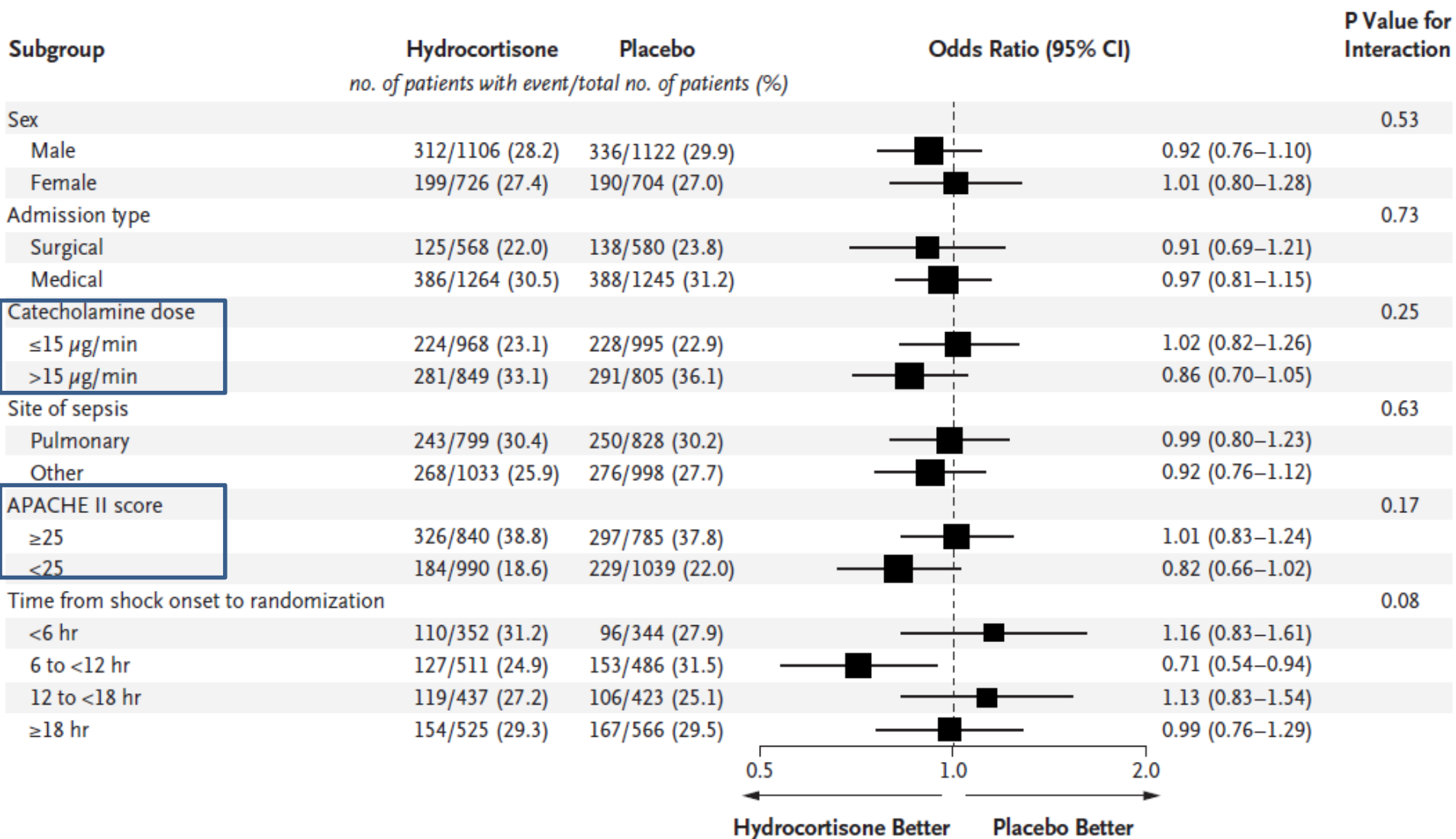
Outcome	Placebo (N=627)	Hydrocortisone plus Fludrocortisone (N=614)	All Patients (N=1241)	Relative Risk (95% CI) [†]	P Value
Primary outcome: death from any cause at day 90 — no. (%)	308 (49.1)	264 (43.0)	572 (46.1)	0.88 (0.78–0.99)	0.03
Secondary outcomes					
Death from any cause					
At day 28 — no. (%)	244 (38.9)	207 (33.7)	451 (36.3)	0.87 (0.75–1.01)	0.06
At ICU discharge — no./total no. (%)	257/627 (41.0)	217/613 (35.4)	474/1240 (38.2)	0.86 (0.75–0.99)	0.04
At hospital discharge — no./total no. (%)	284/627 (45.3)	239/613 (39.0)	523/1240 (42.2)	0.86 (0.76–0.98)	0.02
At day 180 — no./total no. (%)	328/625 (52.5)	285/611 (46.6)	613/1236 (49.6)	0.89 (0.79–0.99)	0.04
Decision to withhold or withdraw active treatment by day 90 — no./total no. (%)	61/626 (9.7)	64/614 (10.4)	125/1240 (10.1)	1.07 (0.77–1.49)	0.69
Vasopressor-free days to day 28 [‡]					
Mean	15±11	17±11	16±11	—	<0.001
Median (IQR)	19 (1–26)	23 (5–26)	21 (2–26)		
Ventilator-free days to day 28 [‡]					
Mean	10±11	11±11	11±11	—	0.07
Median (IQR)	4 (0–21)	10 (0–22)	8 (0–21)		
Organ-failure-free days to day 28 [‡]					
Mean	12±11	14±11	13±11	—	0.003
Median (IQR)	12 (0–24)	19 (0–25)	15 (0–24)		

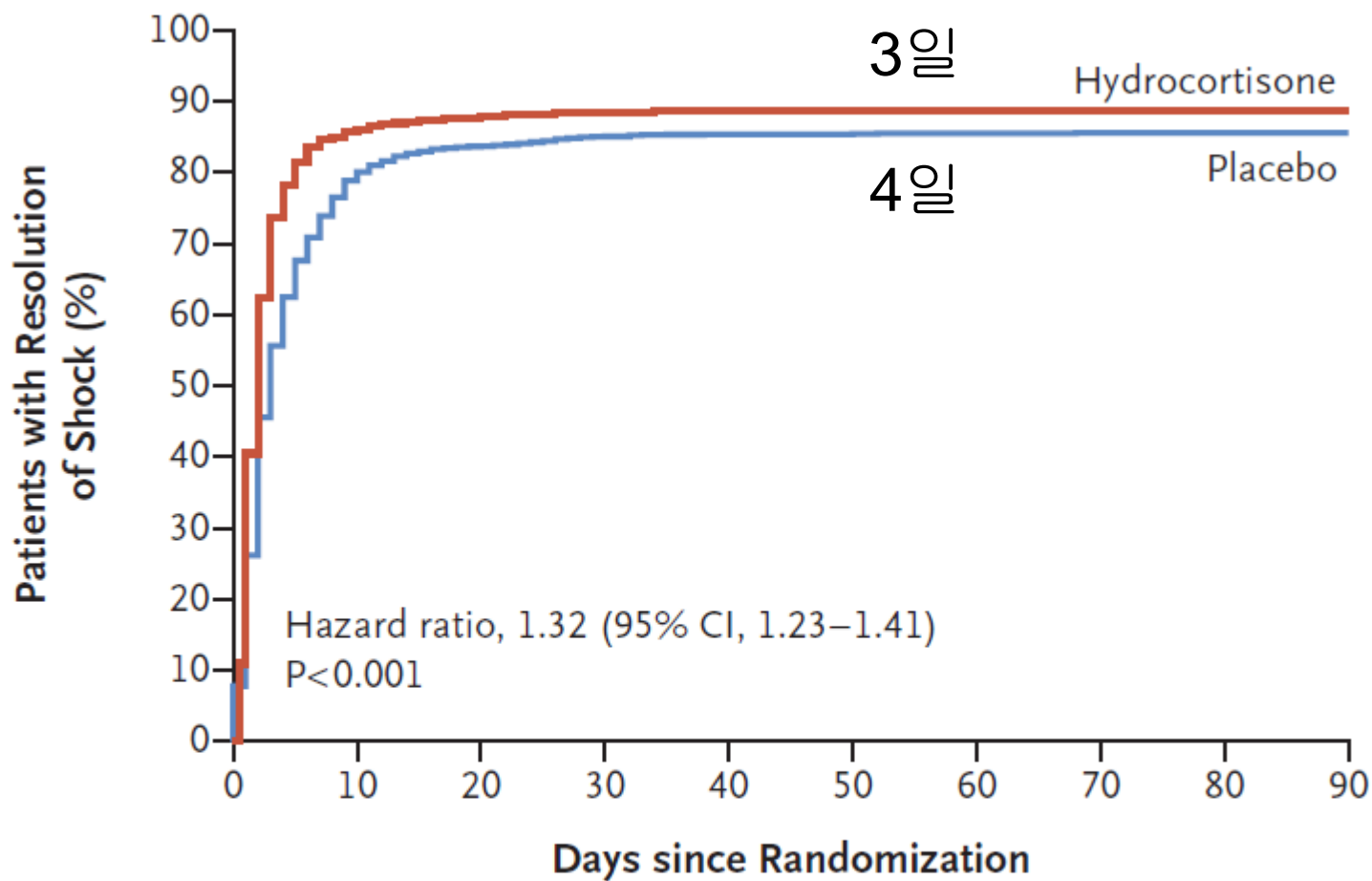
Adjunctive Glucocorticoid Therapy in Patients with Septic Shock (ADRENAL trial)



No. at Risk

Hydrocortisone	1832	1591	1481	1418	1388	1374	1356	1348	1328	1321
Placebo	1826	1546	1433	1376	1354	1337	1330	1322	1312	1300





No. at Risk

Hydrocortisone	1843	104	34	9	6	3	3	2	1	0
Placebo	1854	213	53	19	8	6	4	0	0	0

Renal Replacement Therapy

1. We suggest that either continuous RRT (CRRT) or intermittent RRT be used in patients with sepsis and acute kidney injury
2. We suggest using CRRT to facilitate management of fluid balance in hemodynamically unstable septic patients
3. We suggest *against* the use of RRT in patients with sepsis and acute kidney injury for increase in creatinine or oliguria without other definitive indications for dialysis

Timing of Renal Support and Outcome of Septic Shock and Acute Respiratory Distress Syndrome

Artificial Kidney Initiation in Kidney Injury (AKIKI) trial

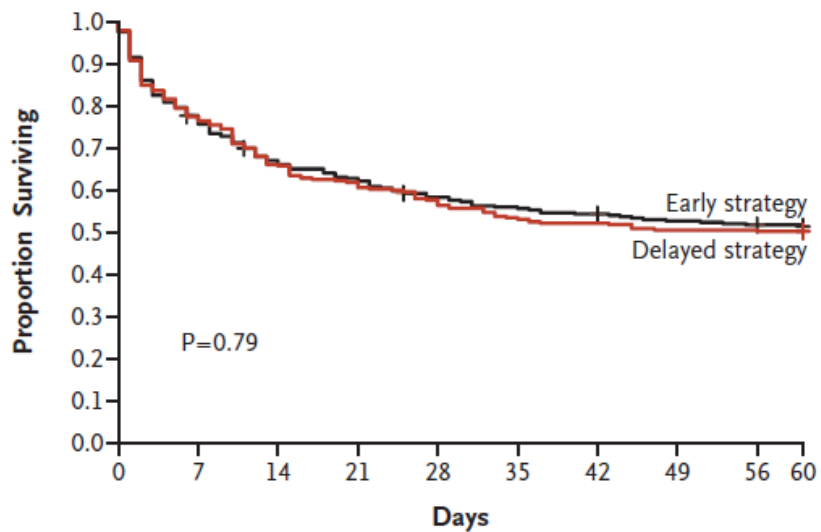
adults (18 years of age or older) admitted to the ICU with AKI
invasive mechanical ventilation and/or catecholamine infusion
have AKI stage 3 of KDIGO classification (at least one of the following criteria)
: serum creatinine concentration of more than 4 mg/dl or
greater than 3 times the baseline creatinine level,
anuria (urine output of 100 ml/day or less) for more than 12 hours,
oliguria (urine output < 0.3 ml/kg/h or < 500 ml/day) for more than 24 hours.

Early strategy

Delayed strategy

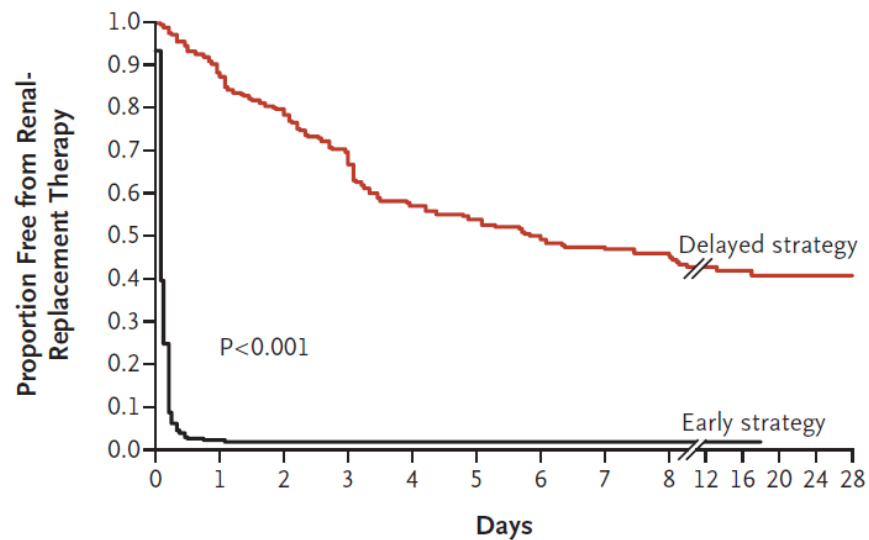
Criteria mandating RRT initiation in the delayed RRT strategy

1. Oliguria or anuria for more than 72 hours after randomization
2. Blood urea nitrogen of more than 112 md/dl (40 mmol/liter)
3. Serum potassium concentration of more than 6 mmol/liter
4. Serum potassium concentration of more than 5.5 mmol/liter despite medical treatment
5. pH below 7.15 in a context of pure metabolic acidosis (PaCO₂ below 35 mmHg) or in a context of mixed acidosis with PaCO₂ of 50 mmHg or more
6. Acute pulmonary edema due to fluid overload responsible for severe hypoxemia



No. at Risk

Early strategy	311	241	207	194	179	172	167	161	158	157
Delayed strategy	308	239	204	191	178	165	161	156	156	155

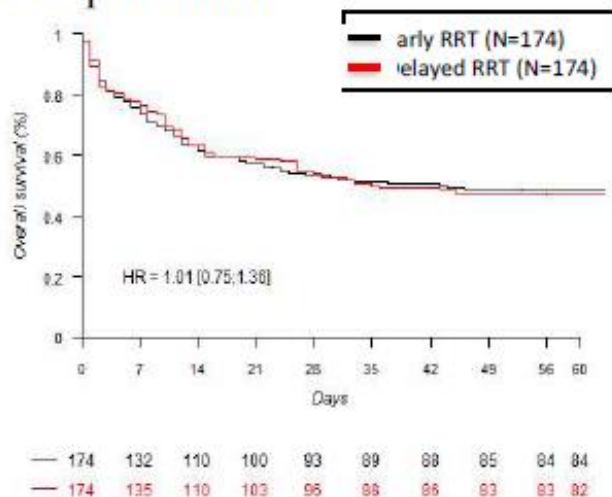


No. at Risk

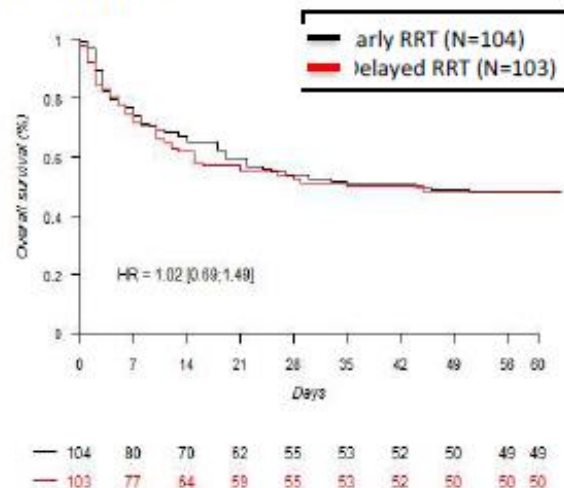
Early strategy	311	7	4	4	4	4	3	3	3	1	1	0	0	0
Delayed strategy	308	268	229	192	153	135	118	105	92	61	39	28	21	13

Subgroup analysis

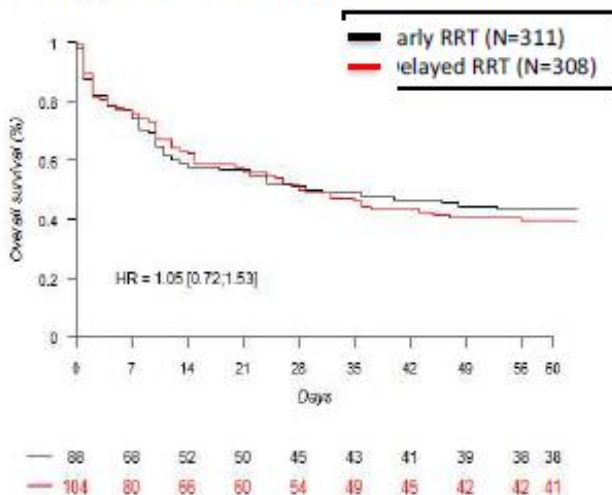
a-Septic Shock



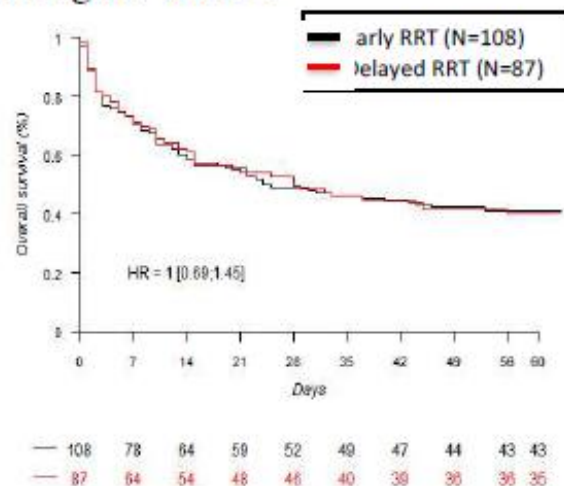
b-ARDS

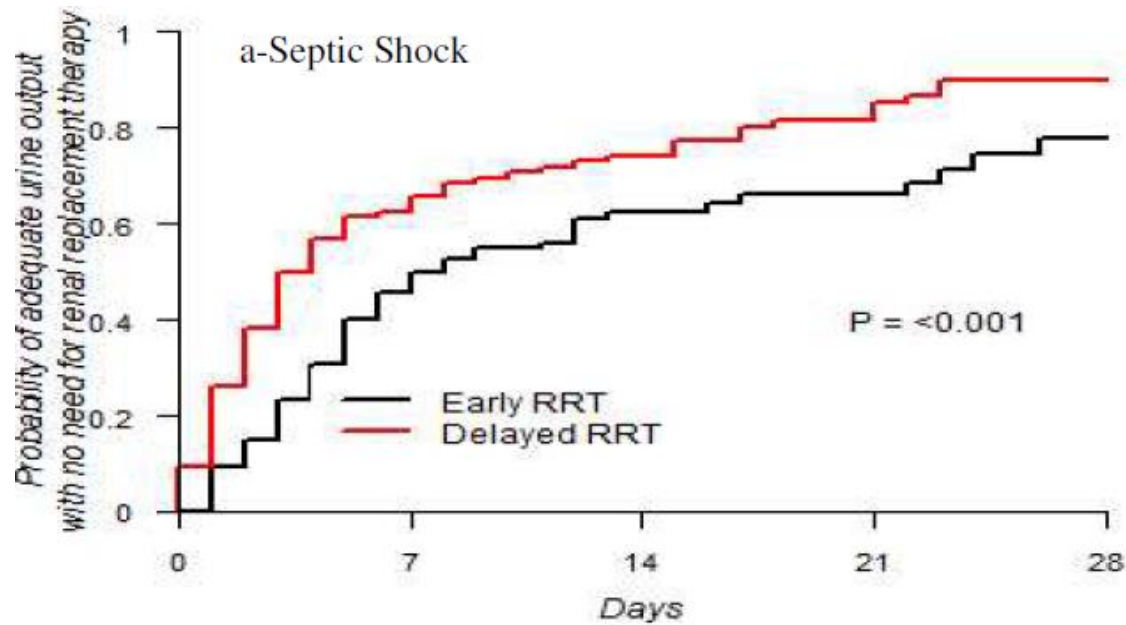


c-Higher SAPS III (vs. [78~138])

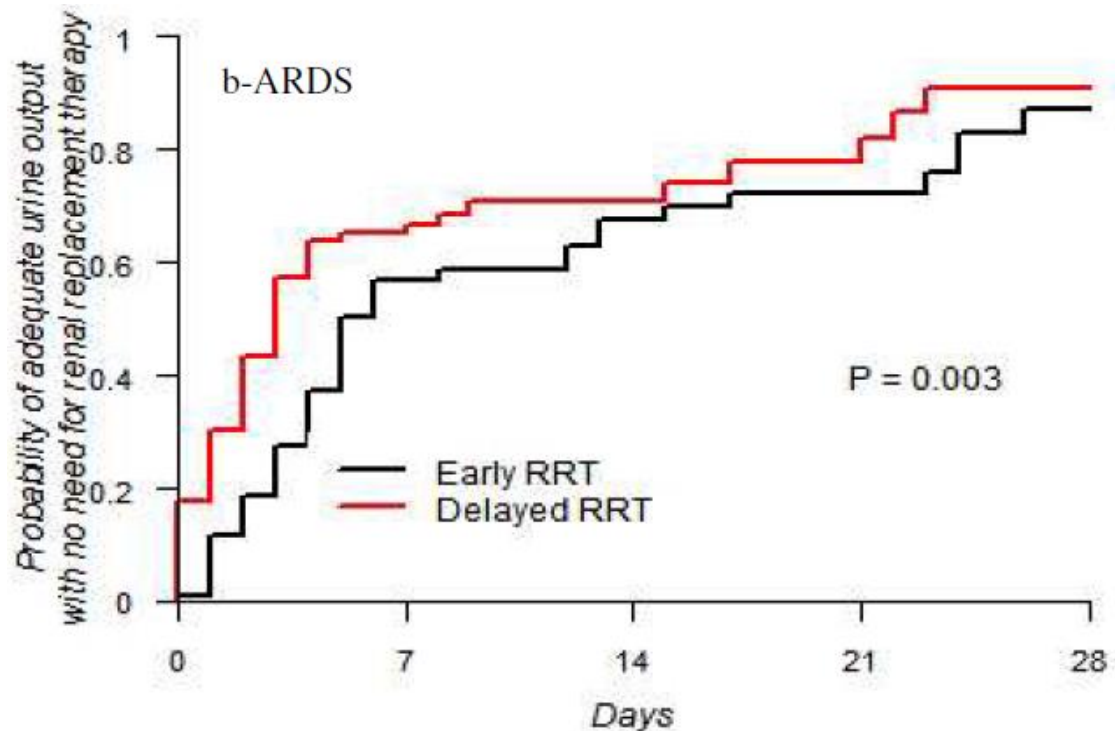


d-Higher SOFA (vs. [13~20])





Delayed strategy group:
45%의 환자가 RRT 를
피함



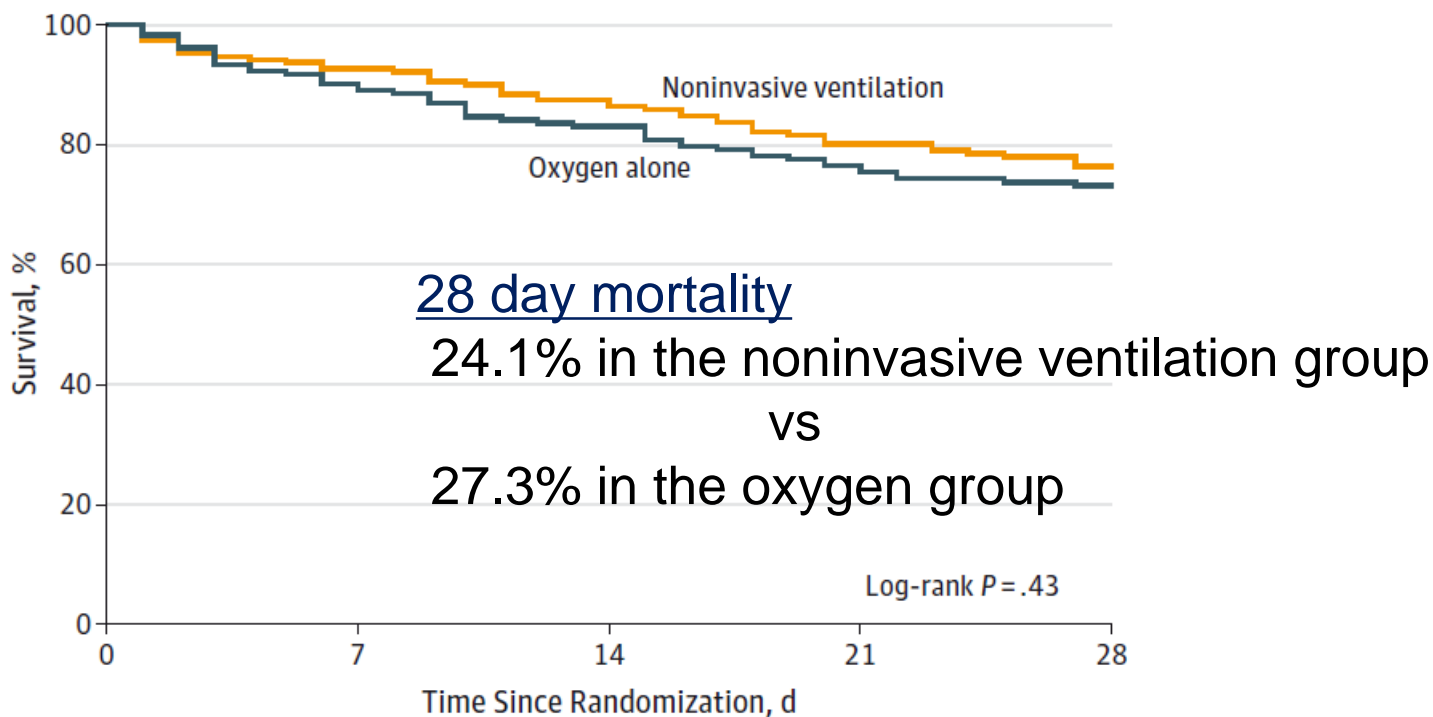
Delayed strategy group:
46%의 환자가 RRT 를
피함



2. RESPIRATORY CARE

Acute hypoxemic respiratory failure in immunocompromised patients: the Efraim multinational prospective cohort study

Effect of Noninvasive Ventilation vs Oxygen Therapy on Mortality Among Immunocompromised Patients With Acute Respiratory Failure
(JAMA. 2015;314:1711-9)



**N=1.611 immunocompromised patients
admitted to 62 ICUs in 16 countries
for acute respiratory failure**

100 with missing data on initial oxygenation strategy

596 (37.0%) received first line intubation and mechanical ventilation (IMV)

915 (56.8%) were not intubated at ICU admission and received standard O₂, noninvasive ventilation (NIV) or high flow oxygen through nasal cannula (HFNC)

O₂
N=496

HFNC
N=187

HFNC + NIV
N=79

NIV
N=153

N=859 without Do-Not-Intubate order

O₂
N=466

HFNC
N=182

HFNC + NIV
N=75

NIV
N=136

N=56 with Do Not Intubate order

IMV: 54 (54%)

IMV: 596 (100%)

IMV: 190 (40.8%)

IMV: 77 (42.3%)

IMV: 32 (42.7%)

IMV: 54 (39.7%)

IMV: 1 (1.8%)

Hospital Mortality:
33% (33 deaths)
Unknown: 6

Hospital Mortality:
52.5% (313 deaths)
Unknown: 22

Hospital Mortality:
34.8% (162 deaths)
Unknown: 15

Hospital Mortality:
37.9% (69 deaths)
Unknown: 14

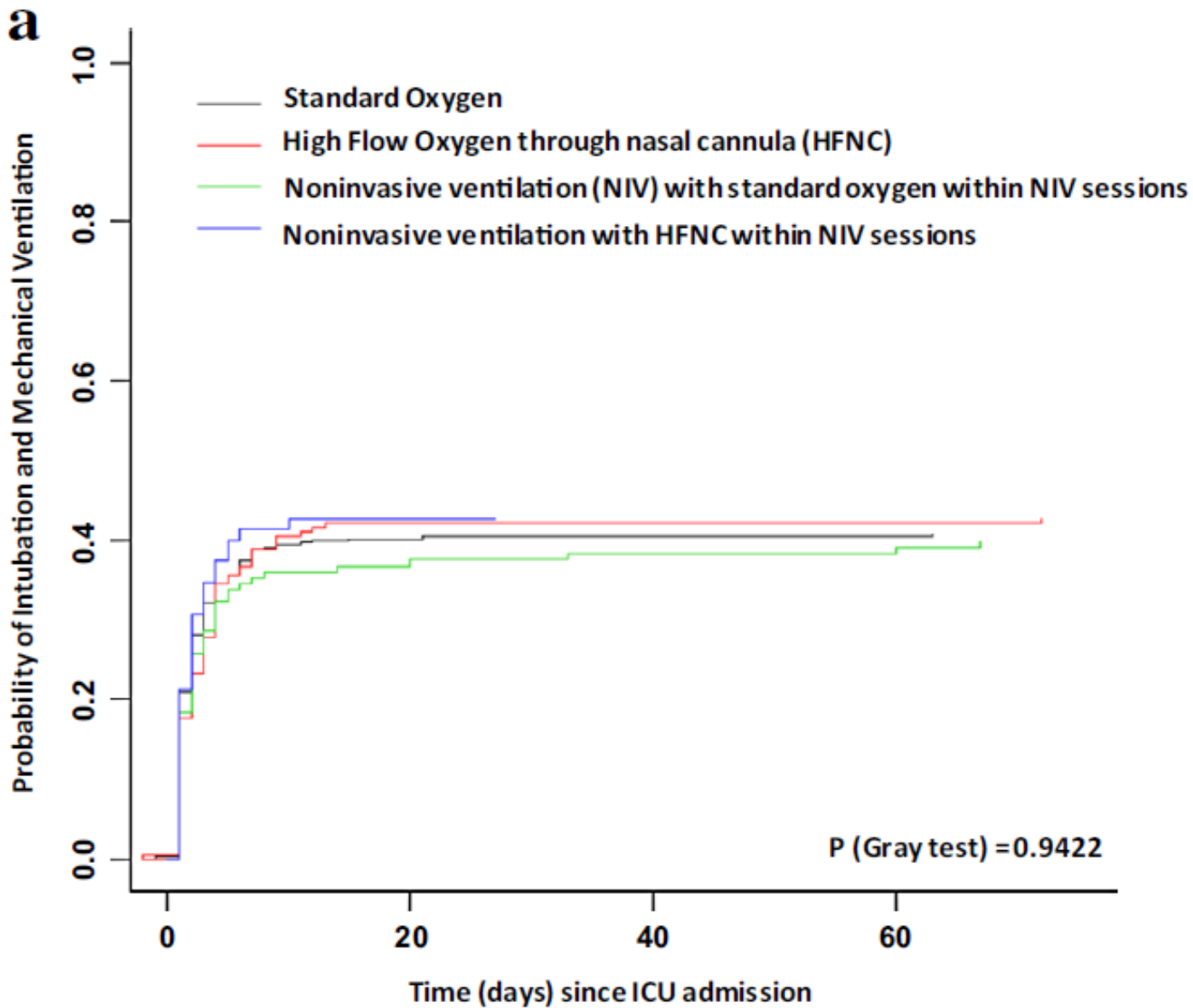
Hospital Mortality:
33.3% (25 deaths)
Unknown: 2

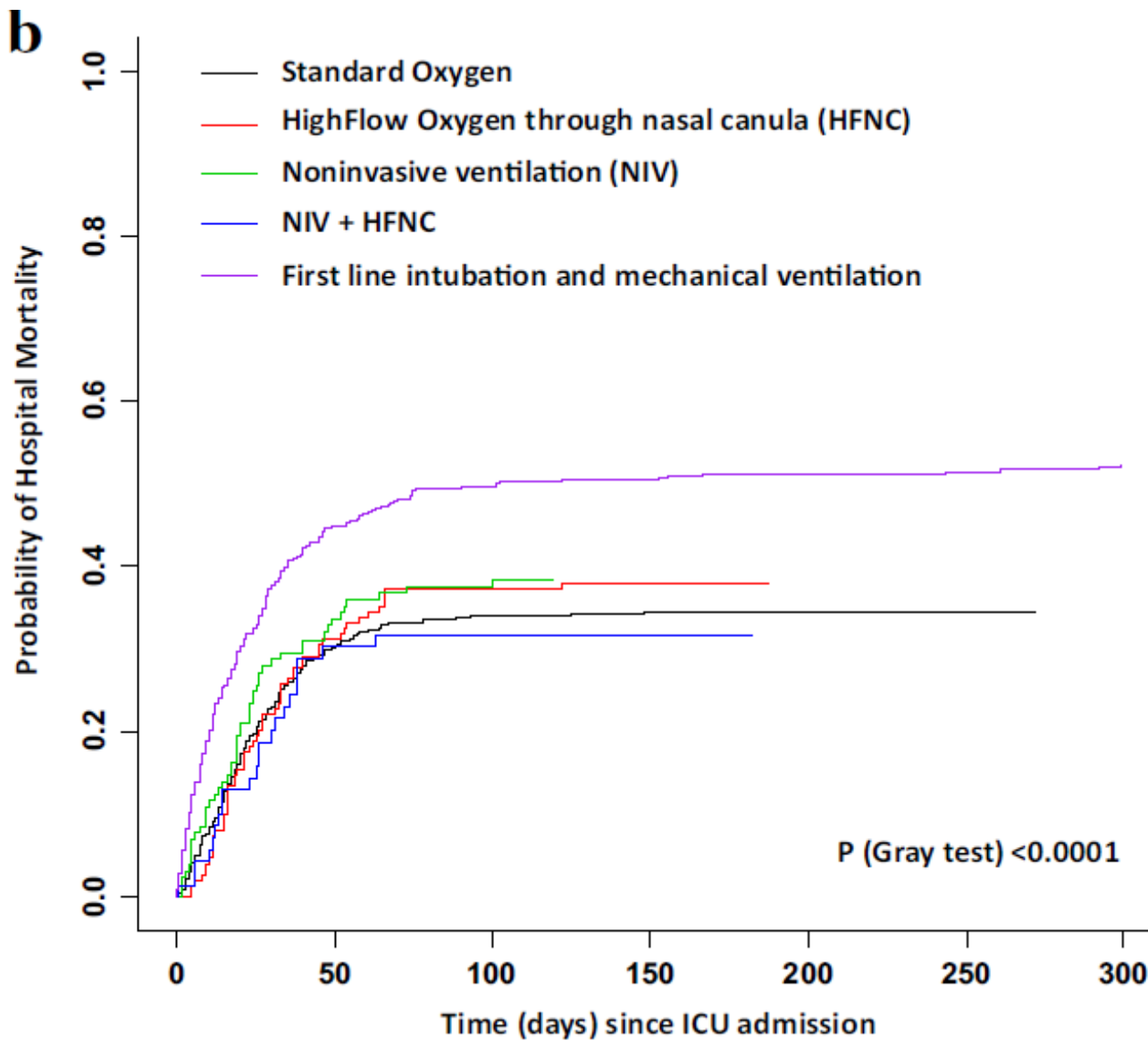
Hospital Mortality:
38.2% (52 deaths)
Unknown: 7

Hospital Mortality:
50% (28 deaths)
Unknown: 0

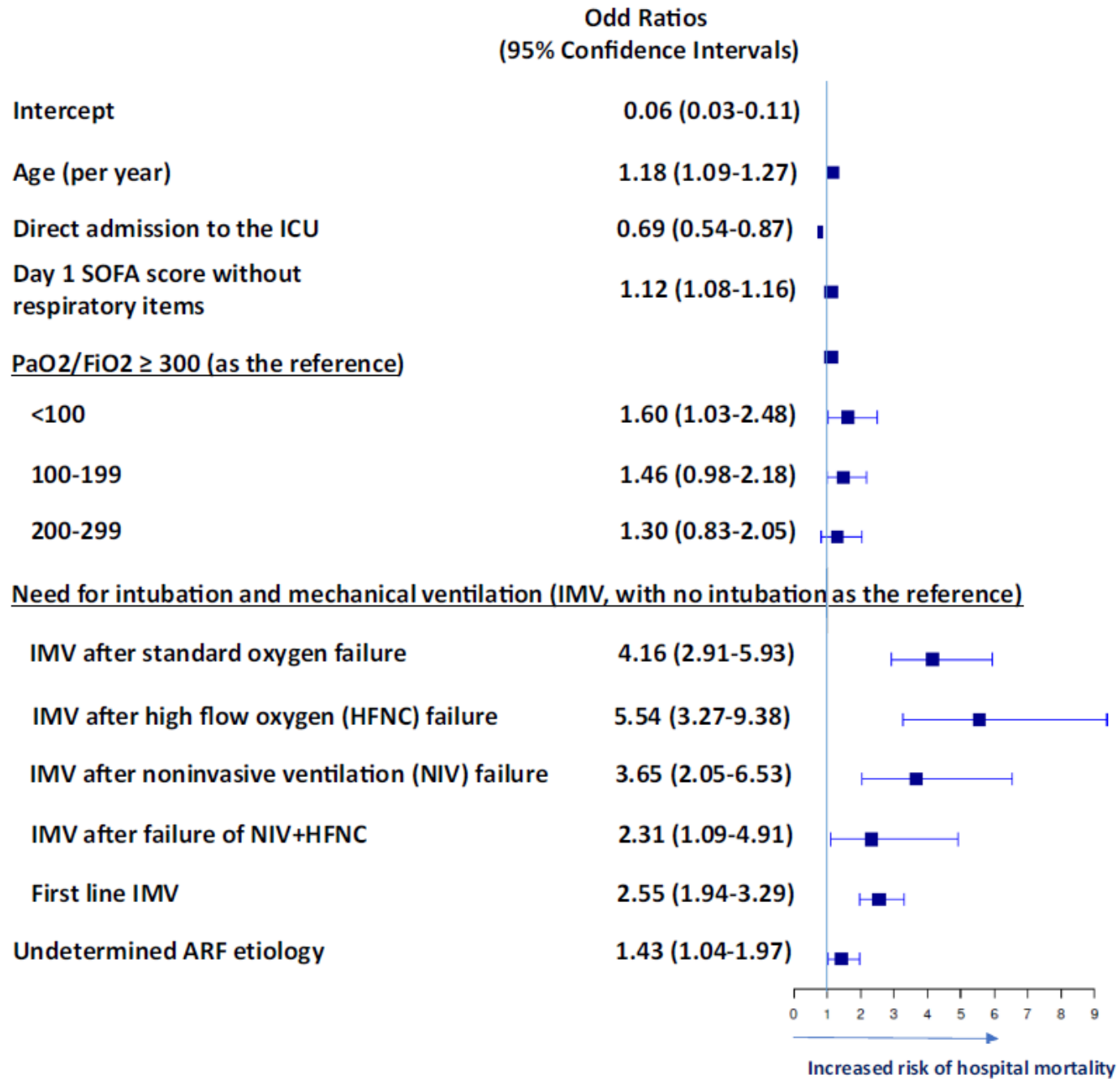
[HFNC ± NIV=257]

[NIV ± HFNC=211]



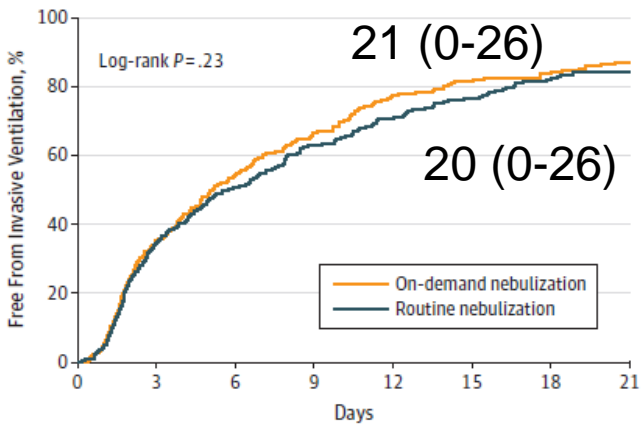


Multivariate model of the prevalence of hospital death (n=1545)



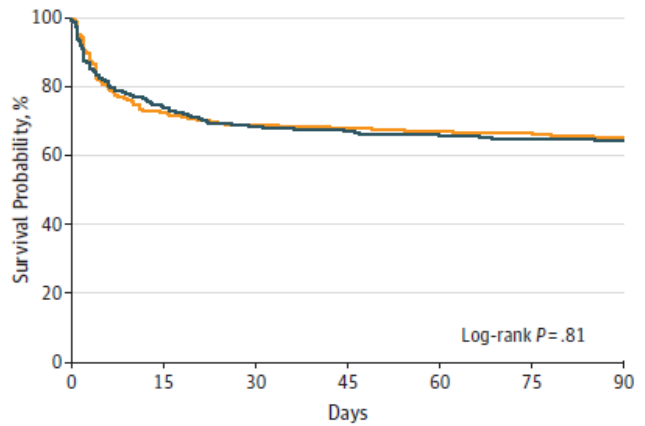
Effect of On-Demand vs Routine Nebulization of Acetylcysteine With Salbutamol on Ventilator-Free Days Intensive Care Unit Patients Receiving Invasive Ventilation

A Freedom from invasive ventilation



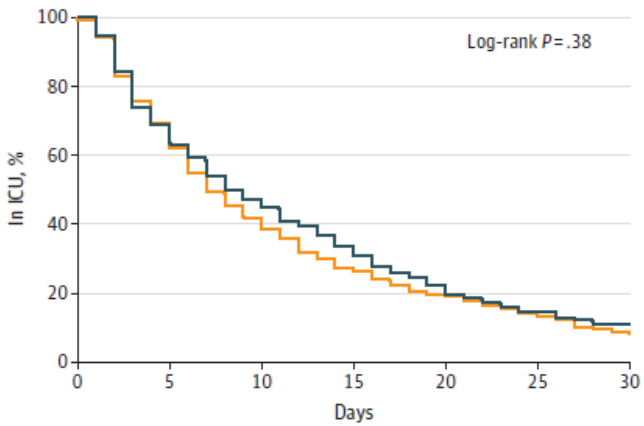
No. at risk								
On-demand	455	252	139	88	53	39	31	23
Routine	467	254	163	108	79	55	37	31

B 90-Day mortality



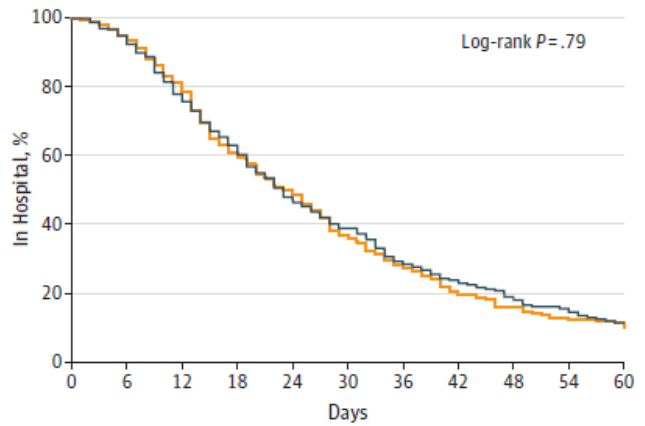
No. at risk								
On-demand	455	330	275	271	267	265	259	
Routine	467	346	285	279	274	270	267	

C ICU Length of stay



No. at risk							
On-demand	455	241	123	71	46	31	16
Routine	467	258	156	99	59	33	18

D Hospital length of stay



No. at risk											
On-demand	455	326	242	167	125	82	60	43	31	24	19
Routine	467	348	258	183	124	95	69	55	40	30	21

Outcome	On-Demand Nebulization (n = 455)	Routine Nebulization (n = 467)	Absolute Difference (95% CI)	P Value ^a
Duration of invasive ventilation, median (IQR)	4 (2-8)	4 (2-10)	-0.5 (-1.3 to 0.2)	.28
Length of stay, median (IQR), d				
ICU	5 (2-10)	5 (2-13)	-0.8 (-1.8 to 0.2)	.49
Hospital	15 (7-27)	14 (6-27)	-0.9 (-3.0 to 1.2)	.57
Pulmonary complications, No. (%) ^c	204 (44.8)	228 (48.8)	-4.0 (-10.4 to 2.4)	.24
Moderate or severe ARDS ^d	23 (5.1)	30 (6.4)	-1.4 (-4.4 to 1.6)	.40
VAP ^e	14 (3.1)	10 (2.1)	0.9 (-1.1 to 3.0)	.41
Severe atelectasis ^f	175 (38.5)	200 (42.8)	-4.4 (-10.7 to 2.0)	.18
Pneumothorax ^g	25 (5.5)	22 (4.7)	0.8 (-2.1 to 3.6)	.65
Tube occlusion ^h	1 (0.2)	2 (0.4)	-0.2 (-0.9 to 0.5)	.99
Adverse events, No. (%) ⁱ	63 (13.8)	137 (29.3)	-15.5 (-20.7 to -10.3)	<.001
Tachyarrhythmia	57 (12.5)	121 (25.9)	-13.4 (-18.4 to -8.4)	<.001
Agitation	1 (0.2)	20 (4.3)	-4.1 (-5.9 to -2.2)	<.001
Hypoxemia	9 (2.0)	20 (4.3)	-2.3 (-4.5 to -0.1)	.06
Dyspnea	1 (0.2)	5 (1.1)	-0.9 (-1.9 to 0.2)	.22
Bronchospasm	1 (0.2)	4 (0.9)	-0.6 (-1.6 to 0.3)	.37
Apnea	0	3 (0.6)	-0.6 (-1.4 to 0.1)	.25
Self-extubation	0	4 (0.9)	-0.9 (-1.7 to 0.0)	.06
Vomiting	1 (0.2)	6 (1.3)	-1.1 (-2.2 to 0.0)	.12

✓
✓
✓
✓

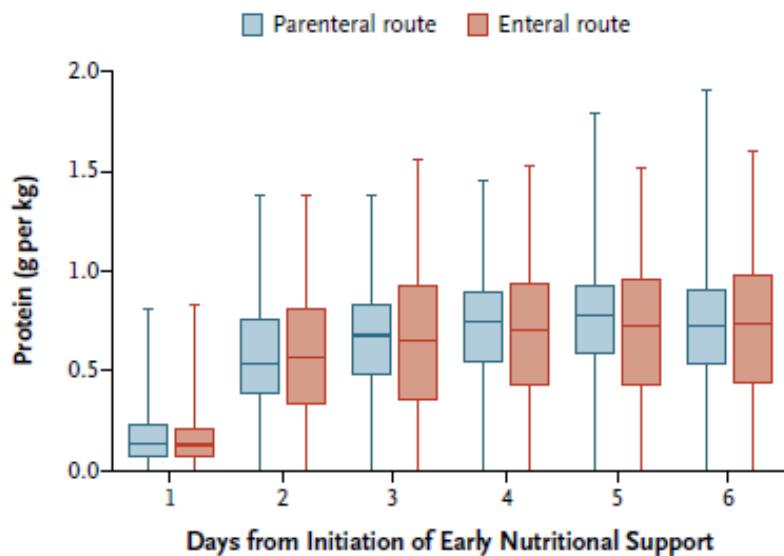


3. NUTRITION

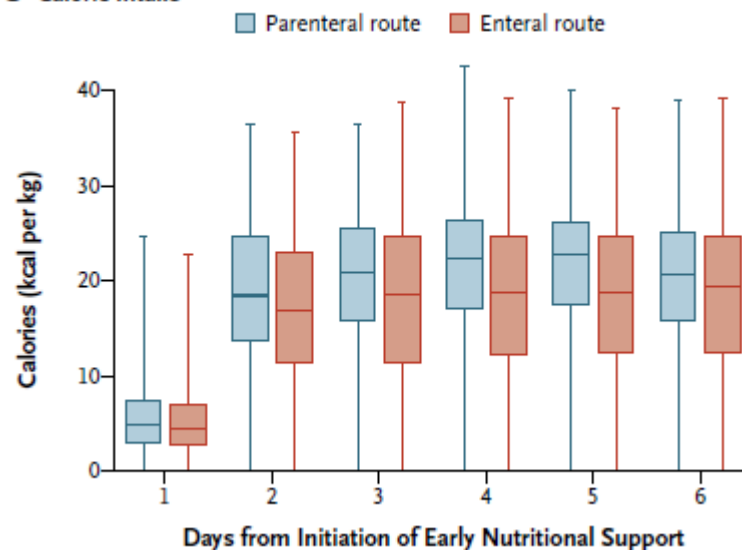
CALORIES Trial

Outcome	Parenteral Group (N=1191)	Enteral Group (N=1197)	Absolute Difference between Groups (95% CI)	Relative Risk (95% CI)	P Value
Primary outcome: death within 30 days — no./total no. (%)	393/1188 (33.1)	409/1195 (34.2)	1.15 (-2.65 to 4.94) [†]	0.97 (0.86 to 1.08) [‡]	0.57 [§]

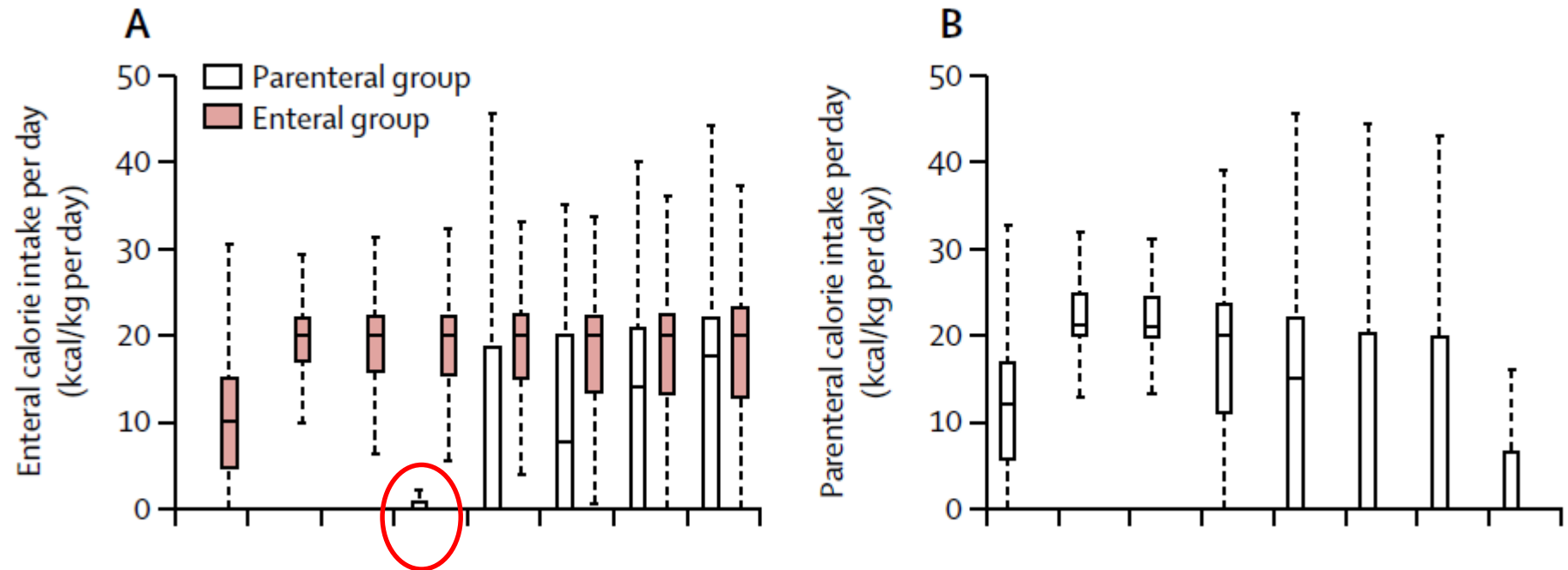
B Protein Intake



C Caloric Intake



Enteral versus parenteral early nutrition in ventilated adults with shock: a randomised, controlled, multicentre, open-label, parallel-group study (NUTRIREA-2)



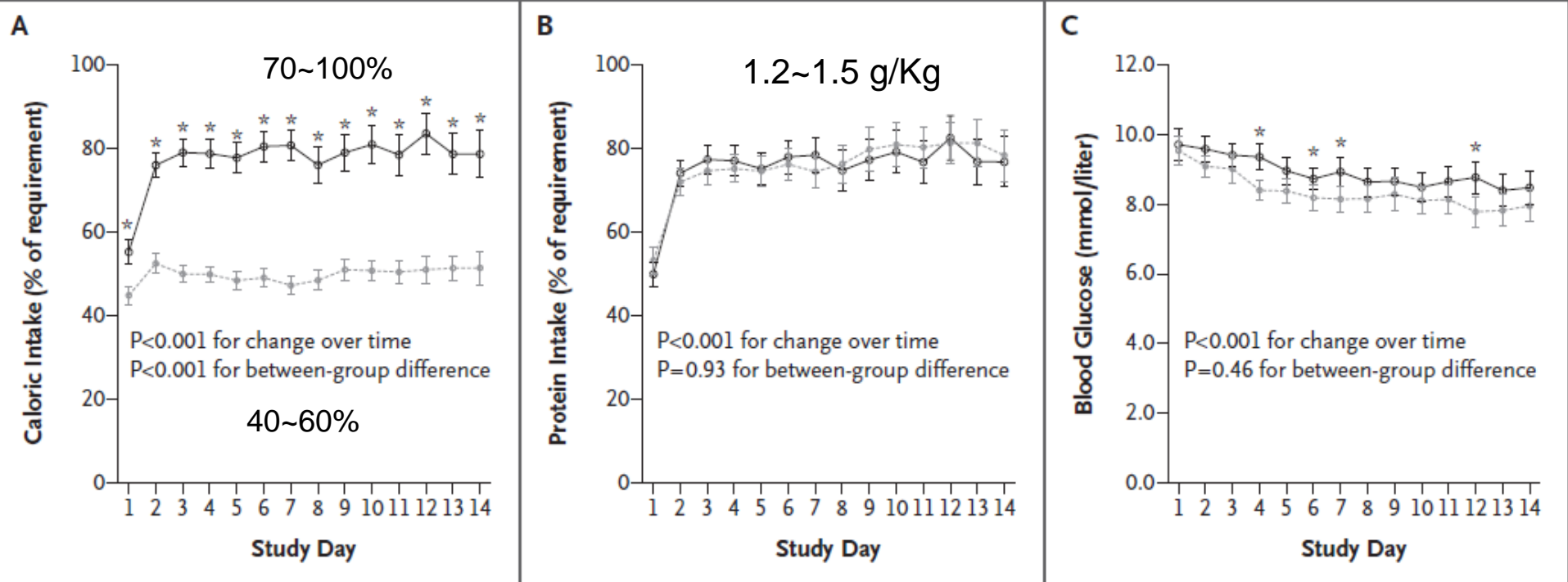
	Enteral group (n=1202)	Parenteral group (n=1208)	Hazard ratio (95% CI)	p value
Days with parenteral nutrition	0.0 (0.0-0.0)	4.0 (3.0-6.0)	..	<0.0001
Days with enteral nutrition	6.0 (3.0-8.0)	1.0 (0.0-3.0)	..	<0.0001
Total calories received (kcal/kg)*	113.5 (61.2)	125.7 (61.9)	..	<0.0001
Daily calorie intake (kcal/kg per 24 h)	17.8 (5.5)	19.6 (5.3)	..	<0.0001
Total protein intake (g/kg)	4.1 (2.3)	5.1 (2.5)	..	<0.0001
Daily protein intake (g/kg/d)	0.7 (0.2)	0.8 (0.2)	..	<0.0001

	Enteral group (n=1202)	Parenteral group (n=1208)	Absolute difference estimate (95% CI)	Hazard ratio (95% CI)	p value
Primary outcome					
Day 28 mortality	443/1202 (37%)	422/1208 (35%)	2.0 (-1.9 to 5.8)	..	0.33
Secondary outcomes					
Day 90 mortality	530/1185 (45%)	507/1192 (43%)	2.2 (-1.8 to 6.2)	..	0.28
ICU mortality*	429 (33%)	405 (31%)	..	1.10 (0.96 to 1.26)	0.17
Hospital mortality*	498 (36%)	479 (34%)	..	1.08 (0.95 to 1.22)	0.25
ICU length of stay (days)	9.0 (5.0 to 16.0)	10.0 (5.0 to 17.0)	0.08
Acute-care hospital length of stay (days)	17.0 (8.0 to 32.0)	18.0 (9.0 to 33.0)	0.11
Days without vasopressor support*	20.0 (0.0 to 25.0)	21.0 (0.0 to 26.0)	0.10
Days without dialysis*	27.0 (0.0 to 28.0)	27.0 (0.0 to 28.0)	0.52
Days without mechanical ventilation*	11.0 (0.0 to 23.0)	12.0 (0.0 to 23.0)	0.54
Infections					
ICU-acquired infection*	173 (14%)	194 (16%)	..	0.89 (0.72 to 1.09)	0.25
Ventilator-associated pneumonia*	113 (9%)	118 (10%)	..	0.96 (0.74 to 1.24)	0.75
Bacteraemia*	38 (3%)	55 (5%)	..	0.69 (0.46 to 1.04)	0.08
CVC-related infection*	29 (2%)	27 (2%)	..	1.07 (0.64 to 1.81)	0.79
Urinary tract infection*	18 (2%)	16 (1%)	..	1.13 (0.58 to 2.21)	0.73
Soft-tissue infection					
Patients (n)	1/1202	6/1208
Other infection*	11 (1%)	21 (2%)	..	0.52 (0.25 to 1.09)	0.08
Gastrointestinal complications					
Vomiting*	406 (34%)	246 (24%)	..	1.89 (1.62 to 2.20)	<0.0001
Diarrhoea*	432 (36%)	393 (33%)	..	1.20 (1.05 to 1.37)	0.009
Bowel ischaemia*	19 (2%)	5 (<1%)	..	3.84 (1.43 to 10.3)	0.007
Acute colonic pseudo-obstruction*	11 (1%)	3 (<1%)	..	3.7 (1.03 to 13.2)	0.04

Permissive Underfeeding or Standard Enteral Feeding in Critically Ill Adults

N Engl J Med 2015;372:2398-408

---○--- Permissive underfeeding —●— Standard feeding



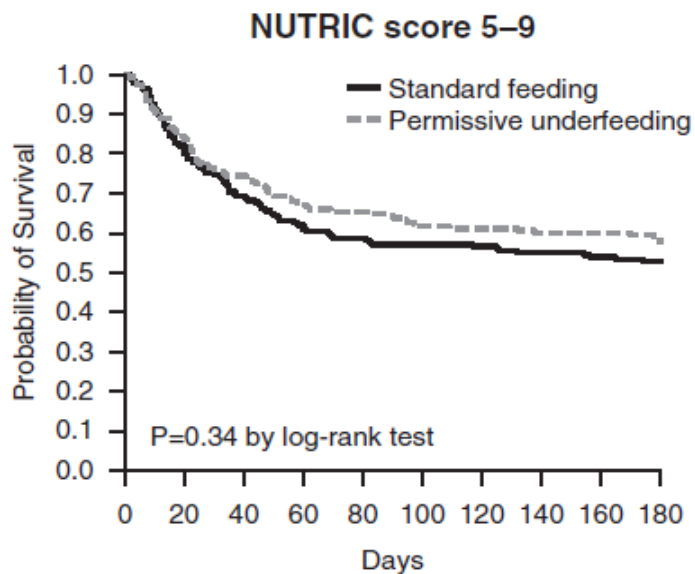
Outcome	Permissive Underfeeding (N = 448)	Standard Feeding (N = 446)	Relative Risk (95% CI)	P Value
Death by 90 days — no./total no. (%)	121/445 (27.2)	127/440 (28.9)	0.94 (0.76–1.16)	0.58
Death in the ICU — no. (%)	72 (16.1)	85 (19.1)	0.84 (0.63–1.12)	0.24
Death by 28 days — no./total no. (%)	93/447 (20.8)	97/444 (21.8)	0.95 (0.74–1.23)	0.7
Death in the hospital — no./total no. (%)	108/447 (24.2)	123/445 (27.6)	0.87 (0.70–1.09)	0.24
Death by 180 days — no./total no. (%)	131/438 (29.9)	140/436 (32.1)	0.93 (0.76–1.14)	0.48

Permissive Underfeeding or Standard Enteral Feeding in High- and Low-Nutritional-Risk Critically Ill Adults. Post Hoc Analysis of the PermiT Trial

Table 1: NUTRIC Score variables

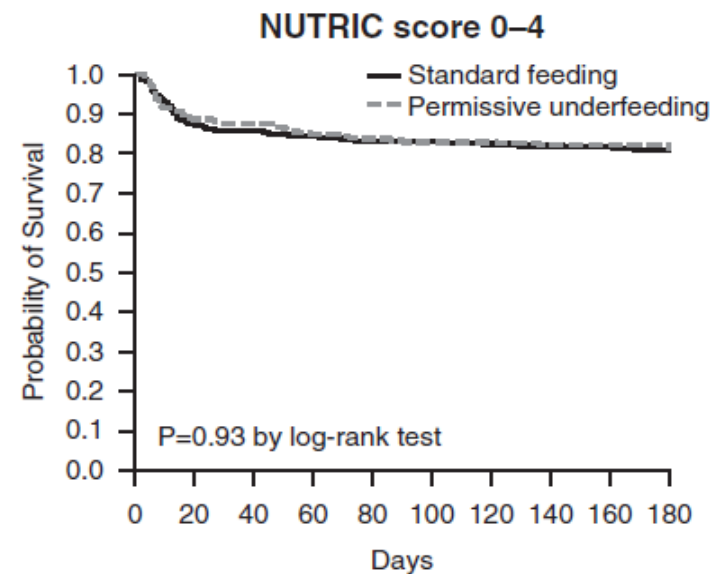
Variable	Range	Points
Age	<50	0
	50 - <75	1
	≥75	2
APACHE II	<15	0
	15 - <20	1
	20-28	2
	≥28	3
SOFA	<6	0
	6 - <10	1
	≥10	2
Number of Co-morbidities	0-1	0
	≥2	1
Days from hospital to ICU admission	0 - <1	0
	≥1	1

**Modified NUTRIC Score
score ≥5 : high score**



No. at Risk

Standard feeding	189	155	131	117	111	108	107	104	102	100
Permissive underfeeding	188	159	140	125	122	115	114	112	112	110



No. at Risk

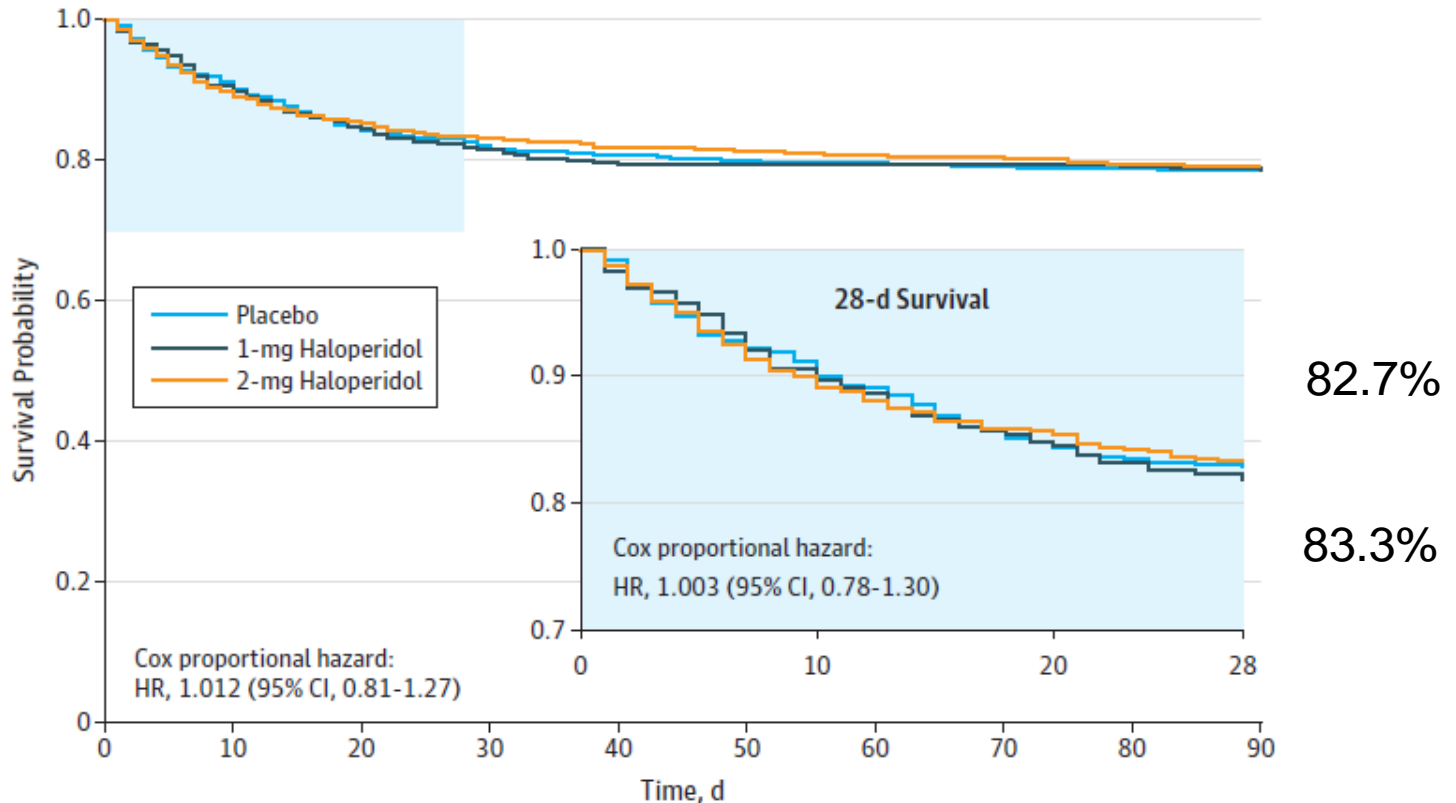
Standard feeding	257	225	221	217	214	214	212	211	210	208
Permissive underfeeding	259	230	227	220	217	215	215	213	213	213



4. DELIRIUM

Effect of Haloperidol on Survival Among Critically Ill Adults With a High Risk of Delirium: The REDUCE Randomized Clinical Trial

Q : the effect of prophylactic haloperidol on survival among critically ill adults ??

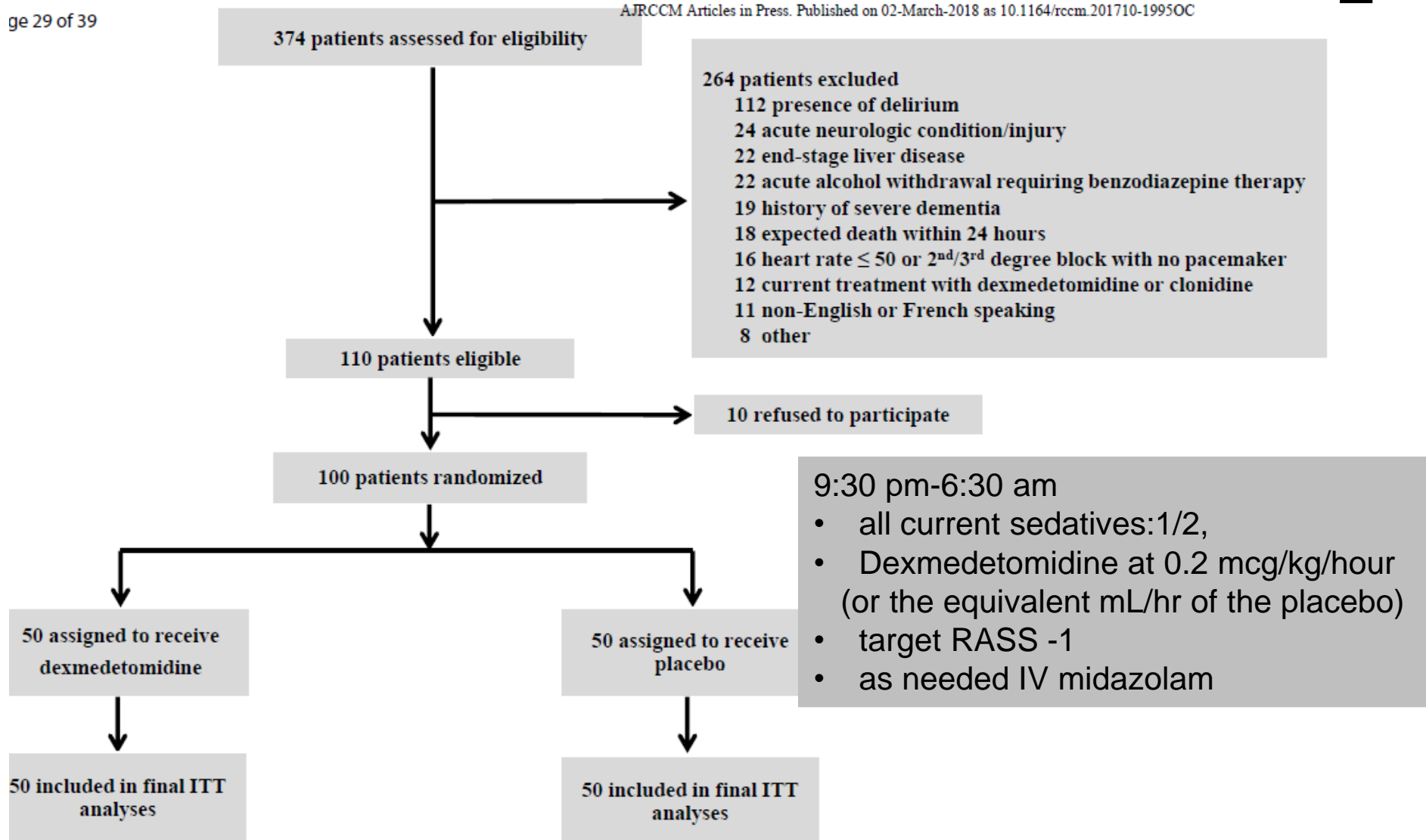


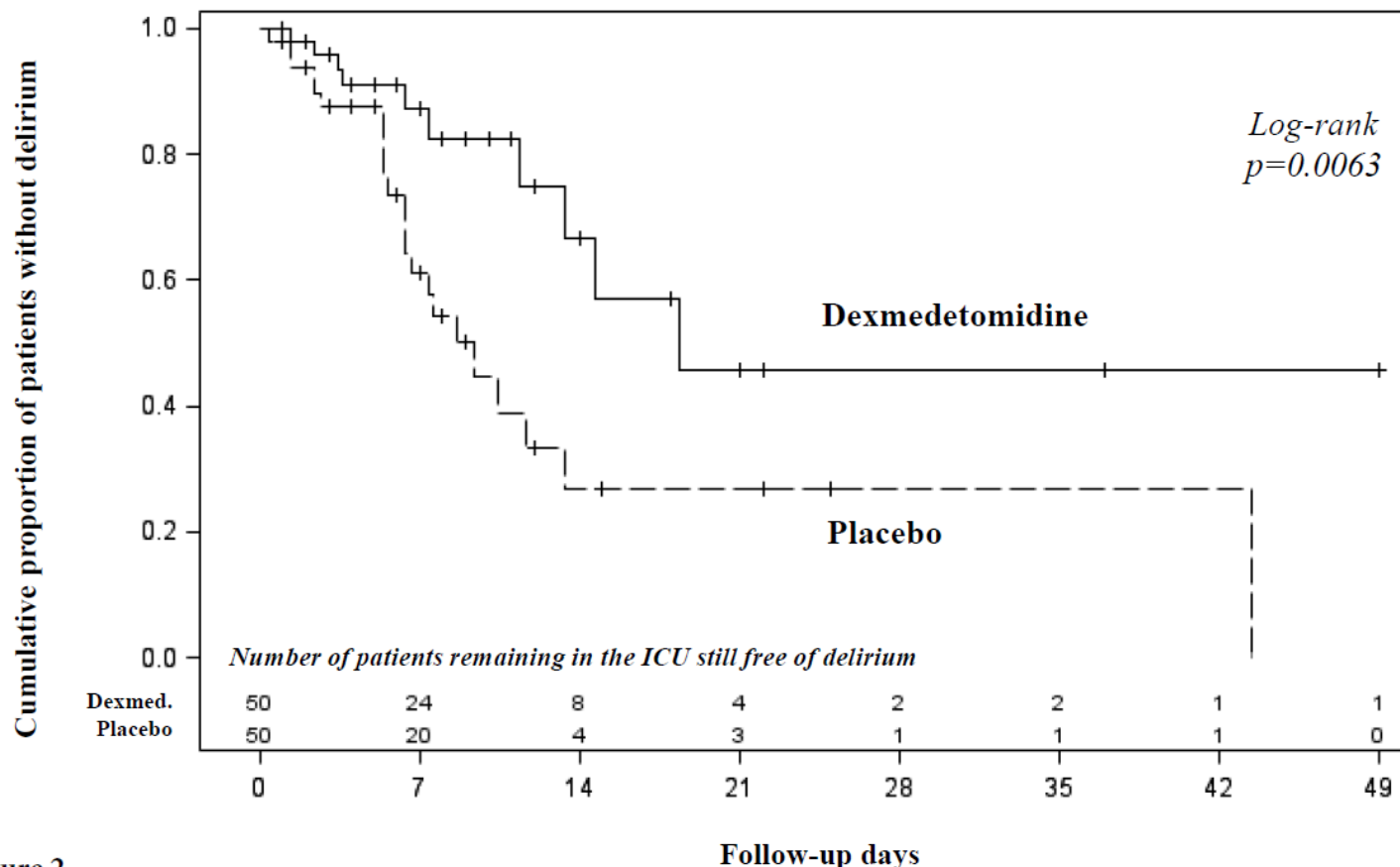
No. at risk	0	10	20	30	40	50	60	70	80	90
Placebo	707	644	600	580	571	565	563	559	557	556
1-mg Haloperidol	350	317	297	285	279	278	278	278	277	276
2-mg Haloperidol	732	658	627	609	599	595	591	589	582	579

Low-dose nocturnal dexmedetomidine prevents ICU delirium: a randomized, placebo-controlled trial

AJRCCM Articles in Press. Published on 02-March-2018 as 10.1164/rccm.201710-1995OC

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Clinical outcomes

Variable	Dexmedetomidine N=50	Placebo N=50	P value
Duration of mechanical ventilation, days	3 [5]	4 [6]	0.94
Duration of ICU stay, days	10 [11]	9 [9]	0.56
ICU mortality, n (%)	9 (18)	6 (12)	0.22
Duration of hospital stay, days	27 [44]	29 [35]	0.48
Hospital mortality, n (%)	13 (26)	11 (22)	0.64