Blood gas Workshop

VTA 2019

Acid

- A substance that dissociates in $H_20 \rightarrow H^+$
- $HCl \rightarrow H^+ + Cl^-$ (complete dissociation)
- Acetic acid $\rightleftharpoons H^+ + Acetate^-$

Base

- Substance that accepts a H^+

Buffer

- Mixture of a weak acid and its conjugate base

Bicarbonate buffer system (ECF)

- H_2C0_3 / $HC0_3^-$
- Strong acid : $HC0_3^- + H^+ \longrightarrow H_2C0_3$
- Strong Base: $H_2C0_3 + OH^- \longrightarrow H_20$

- pH – measure of $[H^+]$ or Log 1/ $[H^+]$
- H/H equation relates the pH of a buffer to the concentration of its buffer acid and base

  pH = pKa + log [base] / [acid]

- $pH = pKa + \log [HC0_3^-] / [H_2C0_3]$
- $pH = 6.1 + \log \quad 20/1$

  $= 7.4$

As long as the ratio 20:1 is kept, irrespective of concentrations, pH is normal

- $H_2C0_3 \rightleftarrows H_20 + C0_2$
- $H_2C0_3 \ \alpha \ pC0_2$

oversimplification

$$\boxed{pH \ \alpha \ [HC0_3^-] / pC0_2}$$

Components of acid base status

- pH α $[HC0_3^-]$ $/pC0_2$

Respiratory component

Non Respiratory component

- If disease causes changes in one component, the other component responds in an attempt to correct the ratio of 20: 1
- See if you can work out the direction of the compensatory component should one component change

Equations

- Metabolic acidosis
- Metabolic alkalosis
- Respiratory acidosis
- Respiratory alkalosis

Delta ratio – Increase in AG / Decrease in HC03

AG calculated- (12) / 24 - (HC03 measured)

Interpretation

<0.4 – Normal AG Met Acid

0.4 – 08 – Mixed Normal AG , High Metabolic Met Acid

1-2 - High AG met Acid

> 2 - HC03 is high to start with

Case 1

pH 7.08
PaCO2 18,8 mmHg
PaO2 100 mmHg
HC03 5,4

Na 136 mmol/l
Cl 102 mmol/l
FiO2 0.3

Case 2

pH 7.48
PaCO2 47 mmHg
PaO2 68 mmHg
HC03 34
FiO2 0.4

K = 2,8

Metabolic Alkalosis

- High pH
- $HC0_3^-$ excess
- Compensation?

$$pH \ \alpha \ [HC0_3^-] / pC0_2$$

Causes of Metabolic alkalosis

- H^+ loss
  - GIT:
    - Vommiting / NG suction
  - Renal:
    - Diuretics
    - Mineralocorticoid excess
    - Low PTH/
    - Post chronic hypercapnea
  - Hypokalemia
    - Transcellular shift/ Loss

- HCO_3 excess
  - $NaHCO_3$ admin
  - Massive transfusion

- Contraction alkalosis

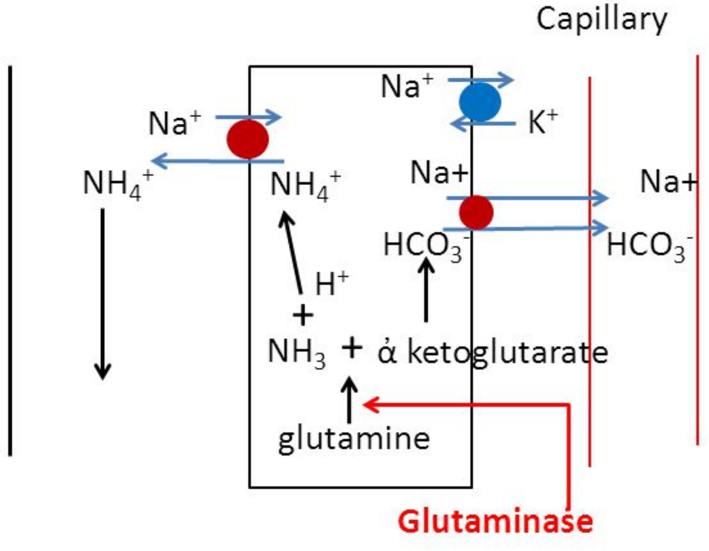
Maintenance of Metabolic alkalosis

- Hypovolemia

Proximal Tubule in H^+ Homeostasis

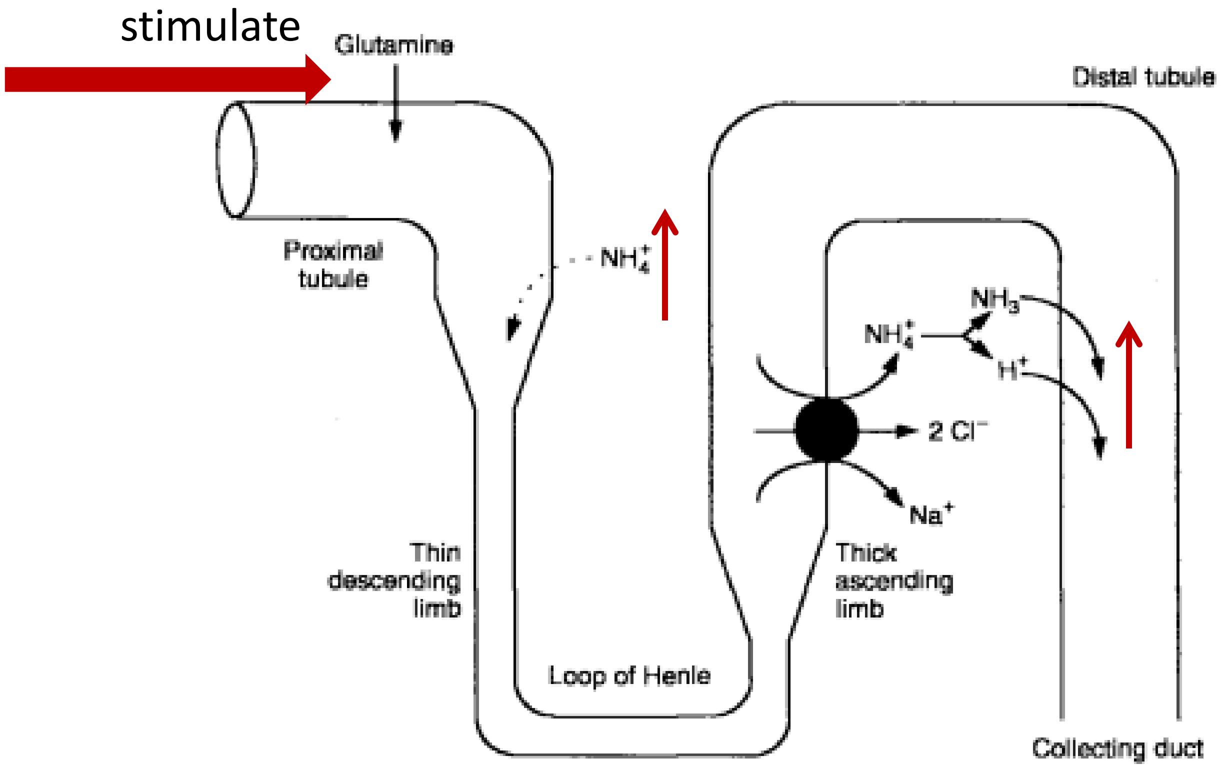
Low ECV
Increased Na reabsorption
Increased NH_4^+ excretion
HCO3 reabsorbtion

Secretion of NH_4^+ by proximal tubular cells



Maintenance of Metabolic alkalosis

- Hypokalemia

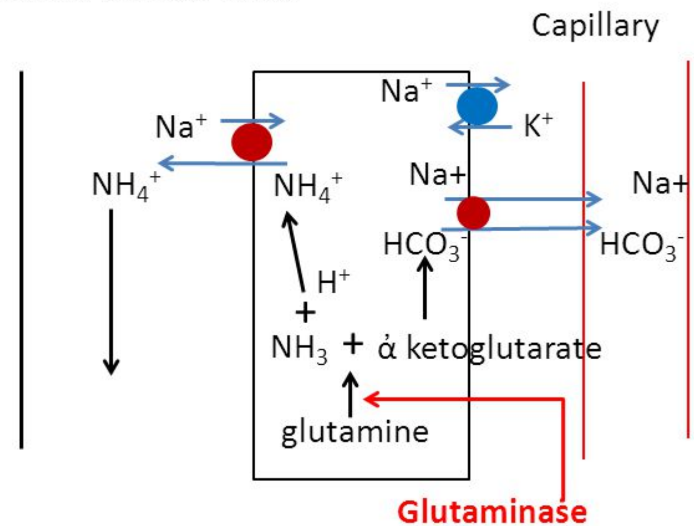


Management

1. Saline responsive
   - Re-expand IVV and break cycle

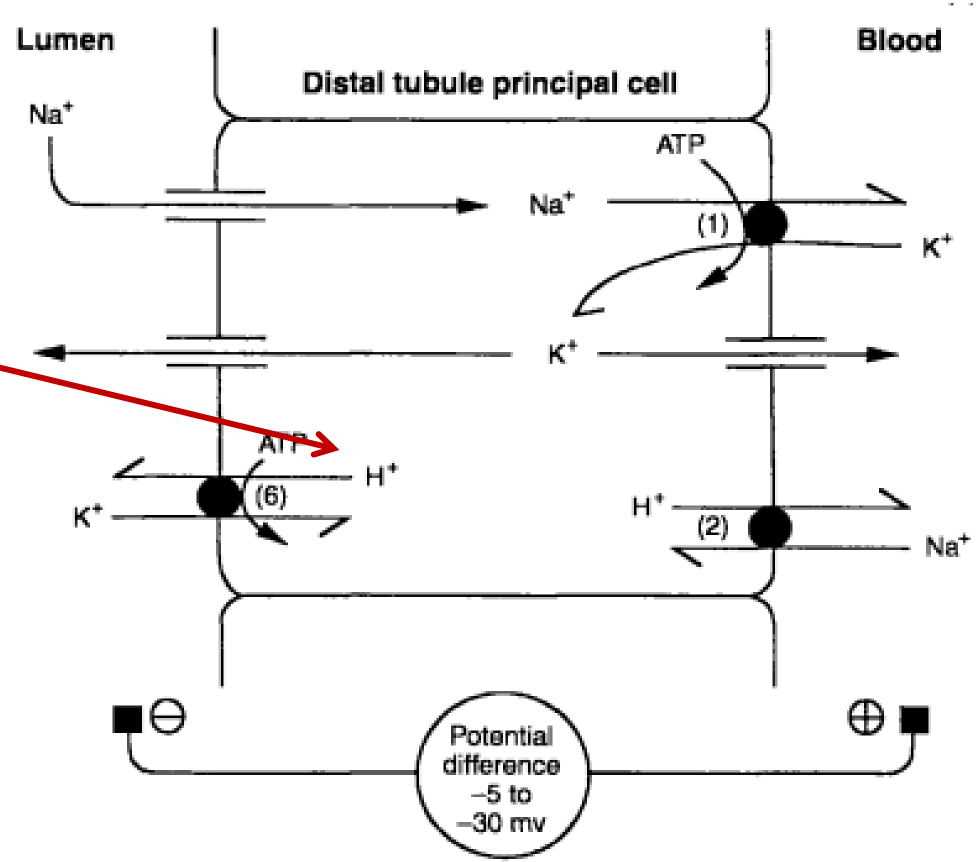
Proximal Tubule in H^+ Homeostasis

Secretion of NH_4^+ by proximal tubular cells



Management

2. Saline resistant
   - Low K driving
   - Plan- Correct K



Case 3

pH 7.50
PaCO2 41 mmHg
PaO2 145 mmHg
HC03 34
FiO2 0.4

K = 2,8

Causes:
1.vomiting in pregnant patient,
2.diuretics or vomiting in patient with chronic respiratory alkalosis typical of cirrhosis,
3. postcardiac arrest (hyperventilation, bicarbonate therapy and conversion of lactate to bicarbonate

Case 4

- Elderly COPD
- pH 7.55
- $PaCO_2$ 53 mmHg
- PaO_2 63 mmHg
- Bicarbonate 48 mmol/l
- FiO_2 0.21

Alveolar arterial gradient

Hypoxemia $PaO_2 < 80$ mmHg

Due to imbalance between:

Pulmonary ventilation and Pulmonary capillary blood flow

$$\boxed{\text{Alveolar } O_2 = FiO_2 \times (\text{Atm Pressure} - H_2O) - PaCO_2/RQ}$$

Decrease if : $PaCO_2$ increases

$PaCO_2 = PaCO_2$ production/ RR x (Vt-Vd)

Case 5

- pH 7.44
- $PaCO_2$ 63 mmHg
- PaO_2 52 mmHg
- Bicarbonate 42 mmol/l
- FiO_2 0.28

A-aDO2

- A-a DO2 in hypoxemia
  1. High:
     - Diffusion/shunt/dead space
  2. Normal: Altitude/Fi02 low or $PaCO_2$ high

Alveolar O_2 = FiO_2 x(Atm Pressure – H_2O) – $PaCO_2$/RQ

- Resp depressants/ sedatives/ms relaxants/NM ds/Skeletal abnormalities

Paeds BASIC ICU Course

- Email:

- paedsbasicjhb@gmail.com

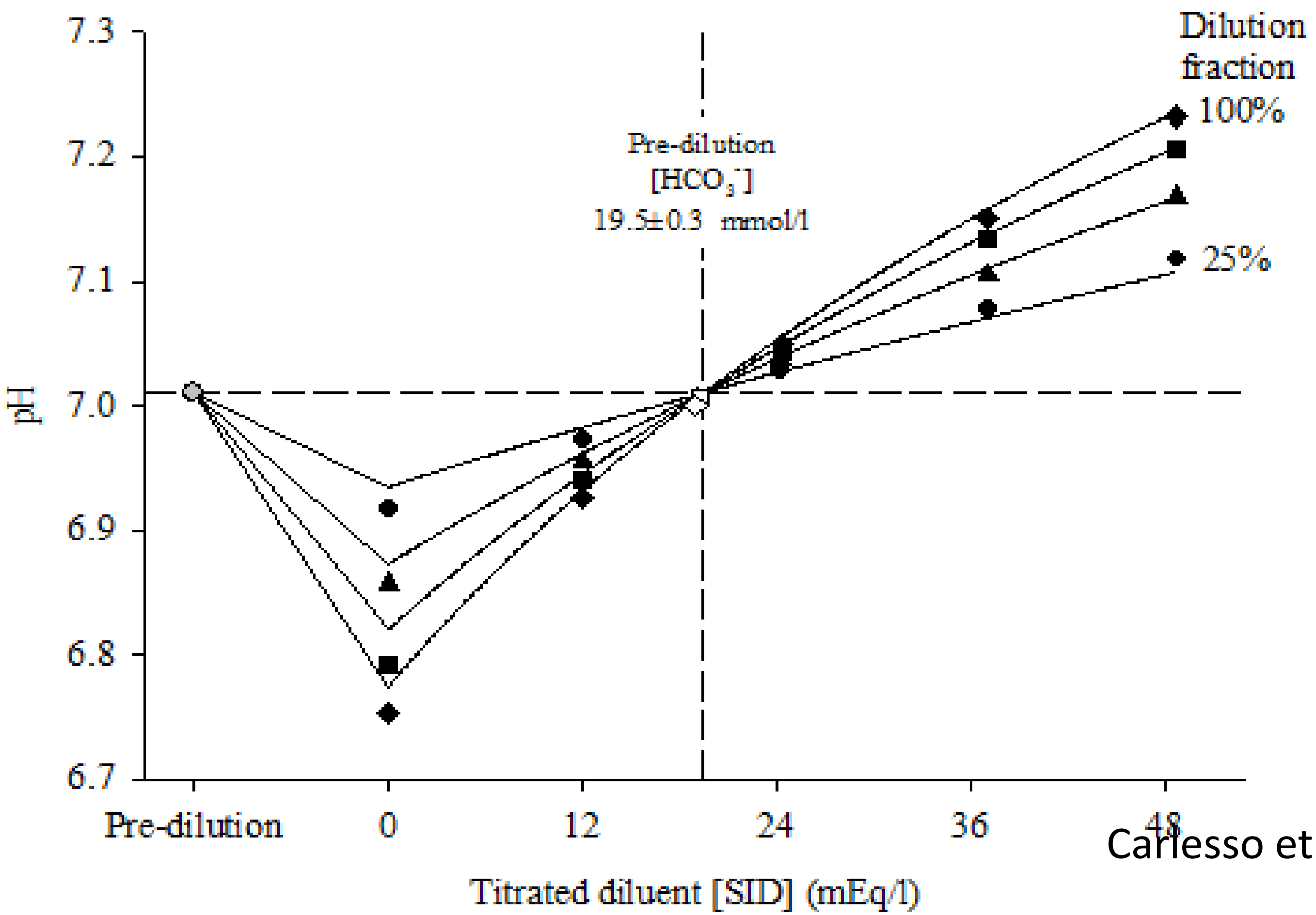
Is Balanced really the solution?

Shahed Omar
University of Witwatersrand/CHBAH

What is balanced?

Content	Plasma	Sodium chloride 0.9%*	Lactated Ringer's (USP)	Ringer's acetate	Alternative balanced solutions for resuscitation**	Bara'lyte
SID (Na+K-Cl)	40	0	28	27	50	52
Na^+ (mmol/l)	135–145	154	130	130	140	142
Cl^- (mmol/l)	95–105	154	109	112	98	99
$[Na^+]:[Cl^-]$ ratio	1.28–1.45:1	1:1	1.19:1	1.16:1	1.43:1	1.43:1
K^+ (mmol/l)	3.5–5.3	*	4	5	5	3.6
HCO_3^- / Bicarbonate	24–32	0	28 (lactate)	27 (acetate)	27 (acetate) 23 (gluconate)	49
Ca^2+ (mmol/l)	2.2–2.6	0	1.4	1	0	0
Mg^2+ (mmol/l)	0.8–1.2	0	0	1	1.5	2.7
Glucose (mmol/ l)	3.5–5.5	0	0	0	0	0
pH	7.35–7.45	4.5–7.0	6–7.5	6–8	4.0–8.0	
Osmolarity (mOsm/l)	275–295	308	273	276	295	296

Balanced- depends on what you want



Carlesso et al (ICM 2010

Respiration Physiology (1978) **33**, 9–26

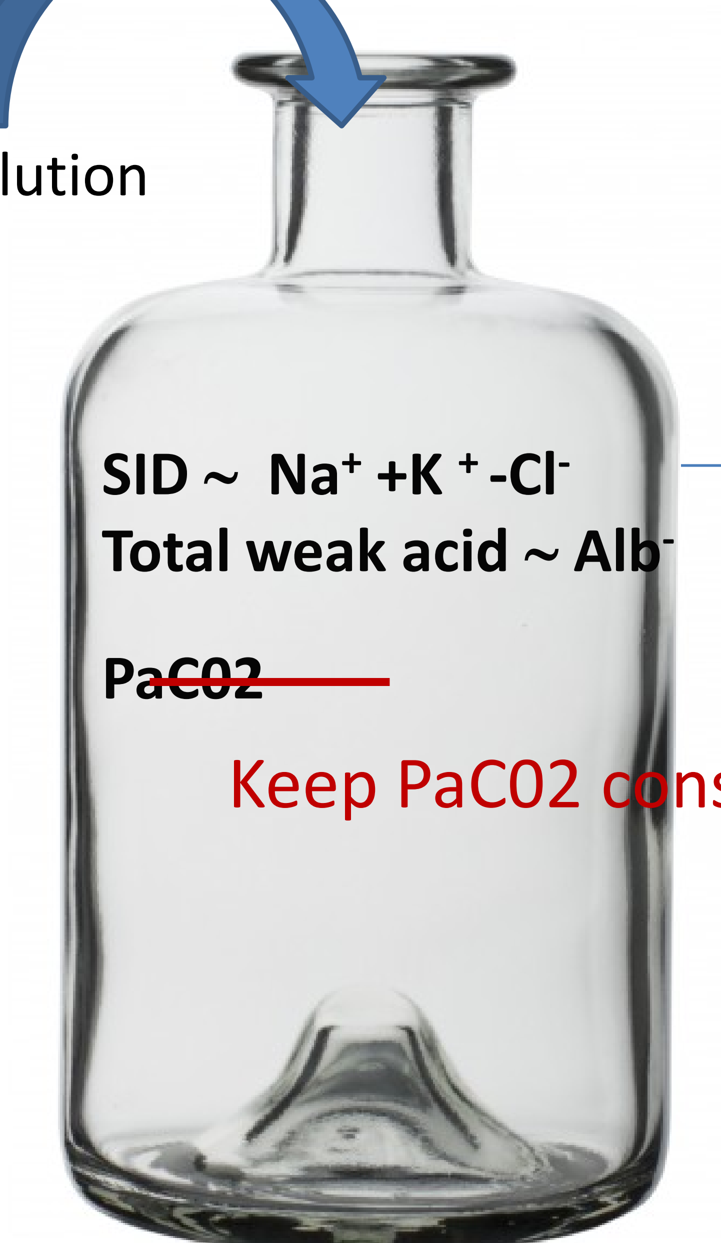
INDEPENDENT AND DEPENDENT VARIABLES OF ACID–BASE CONTROL[1]

PETER A. STEWART

Physiology/Biophysics, Brown University. Providence, Rhode Island 02912, U.S.A.

Perfect solution

SID = 24



SID ~ Na^{+} +K^{+} -Cl^{-}

Total weak acid ~ Alb^{-}

~~PaC02~~

Keep PaC02 constant

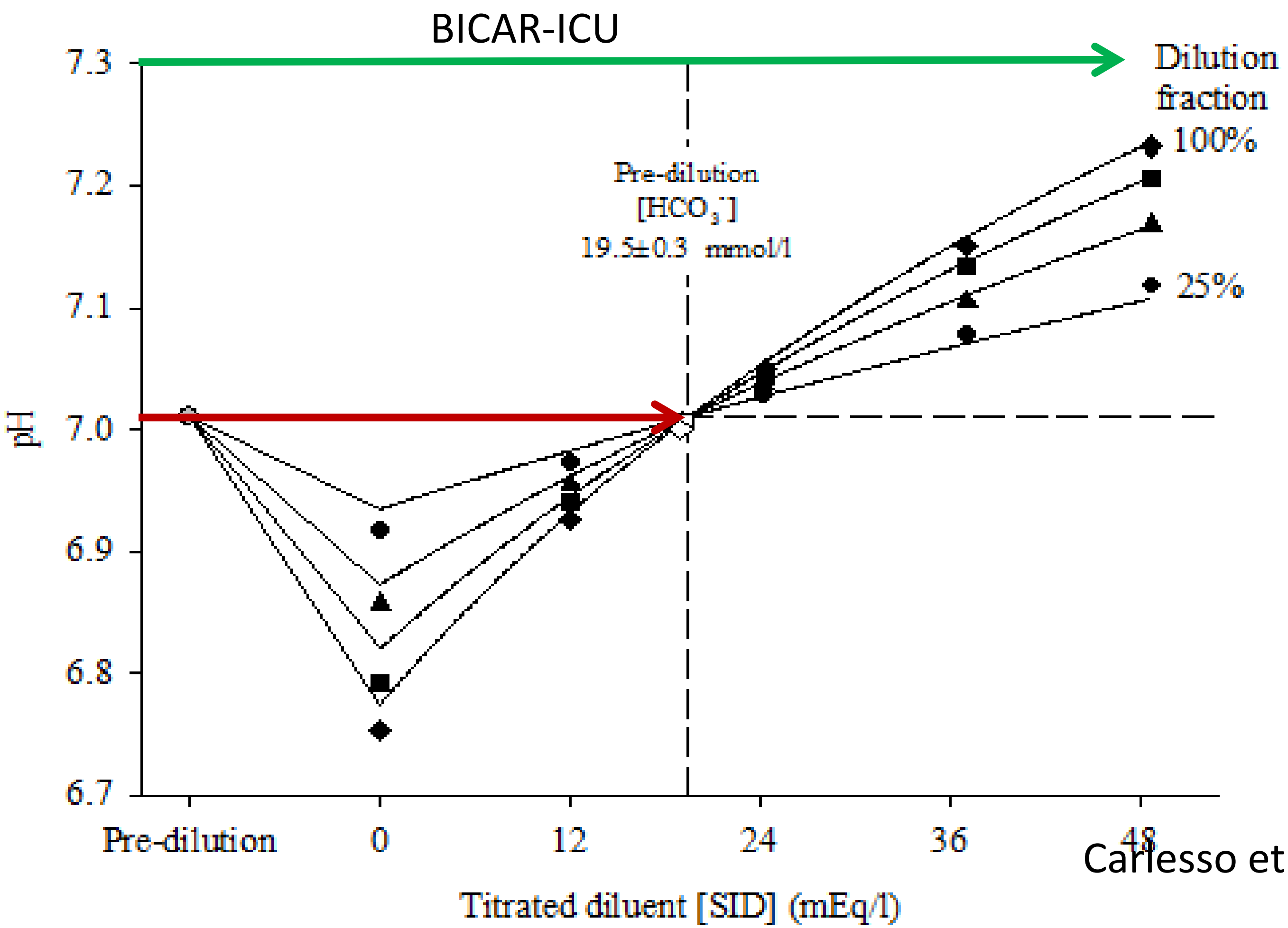
No effect on pH

Reduction the SID - ↑**H^{+}**

=

Reduction the Total weak $acid^{-}$ ↓**H^{+}**

Balanced- depends on what you want



Carlesso et al (ICM 2010

Sodium bicarbonate therapy for patients with severe metabolic acidaemia in the intensive care unit (BICAR-ICU): a multicentre, open-label, randomised controlled, phase 3 trial

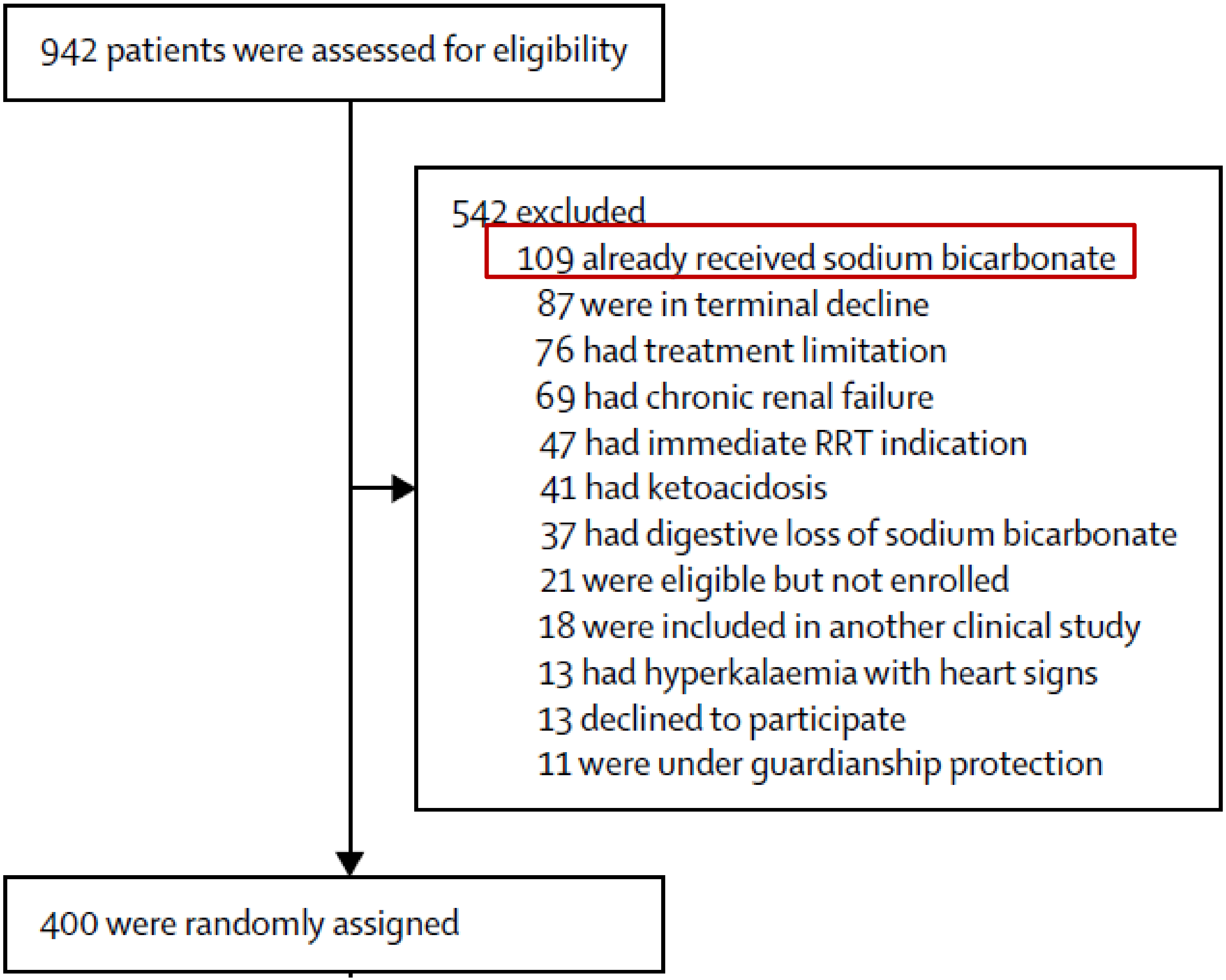
*Samir Jaber, Catherine Paugam, Emmanuel Futier, Jean-Yves Lefrant, Sigismond Lasocki, Thomas Lescot, Julien Pottecher, Alexandre Demoule, Martine Ferrandière, Karim Asehnoune, Jean Dellamonica, Lionel Velly, Paër-Sélim Abback, Audrey de Jong, Vincent Brunot, Fouad Belafia, Antoine Roquilly, Gérald Chanques, Laurent Muller, Jean-Michel Constantin, Helena Bertet, Kada Klouche, Nicolas Molinari, Boris Jung, for the BICAR-ICU Study Group**

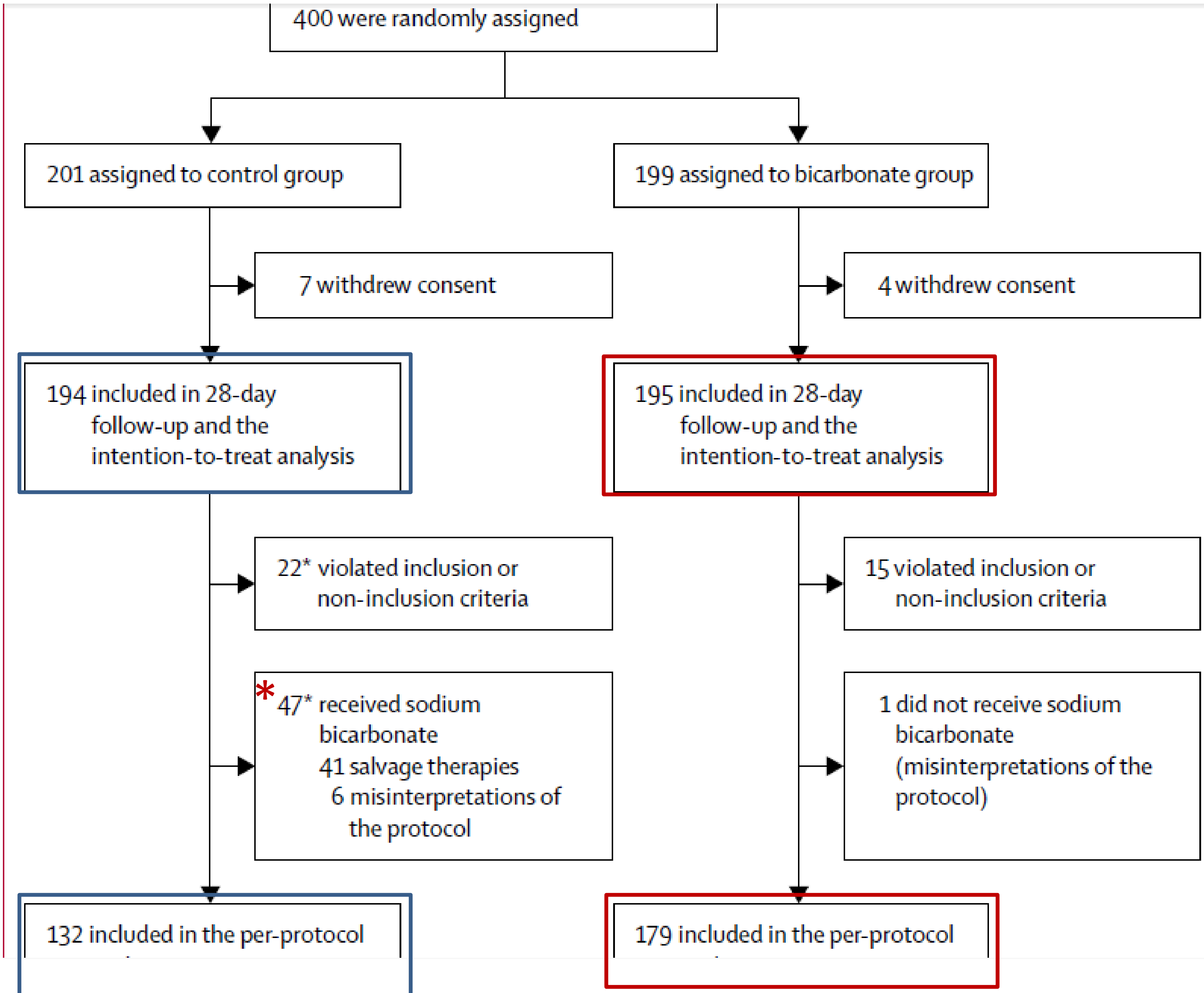
Hypothesized

Early NaHC03 infusion vs no NaHC03 would result the composite of fewer deaths (D28) and SOFA 1by D7

Lancet 2018

- Inclusion (All)
  - ≥ 18y
  - Within 48h of ICU admission
  - pH≤ 7.2 and PaC02 ≤ 45
  - SOFA ≥ 4 or Lac ≥ 2
- Exclusion
  - Resp Acidosis/ HC03 loss from GIT or kidney
  - CKD – 4
  - Ketoacidosis
  - NaHC03 Rx or RRT within 24 of screening

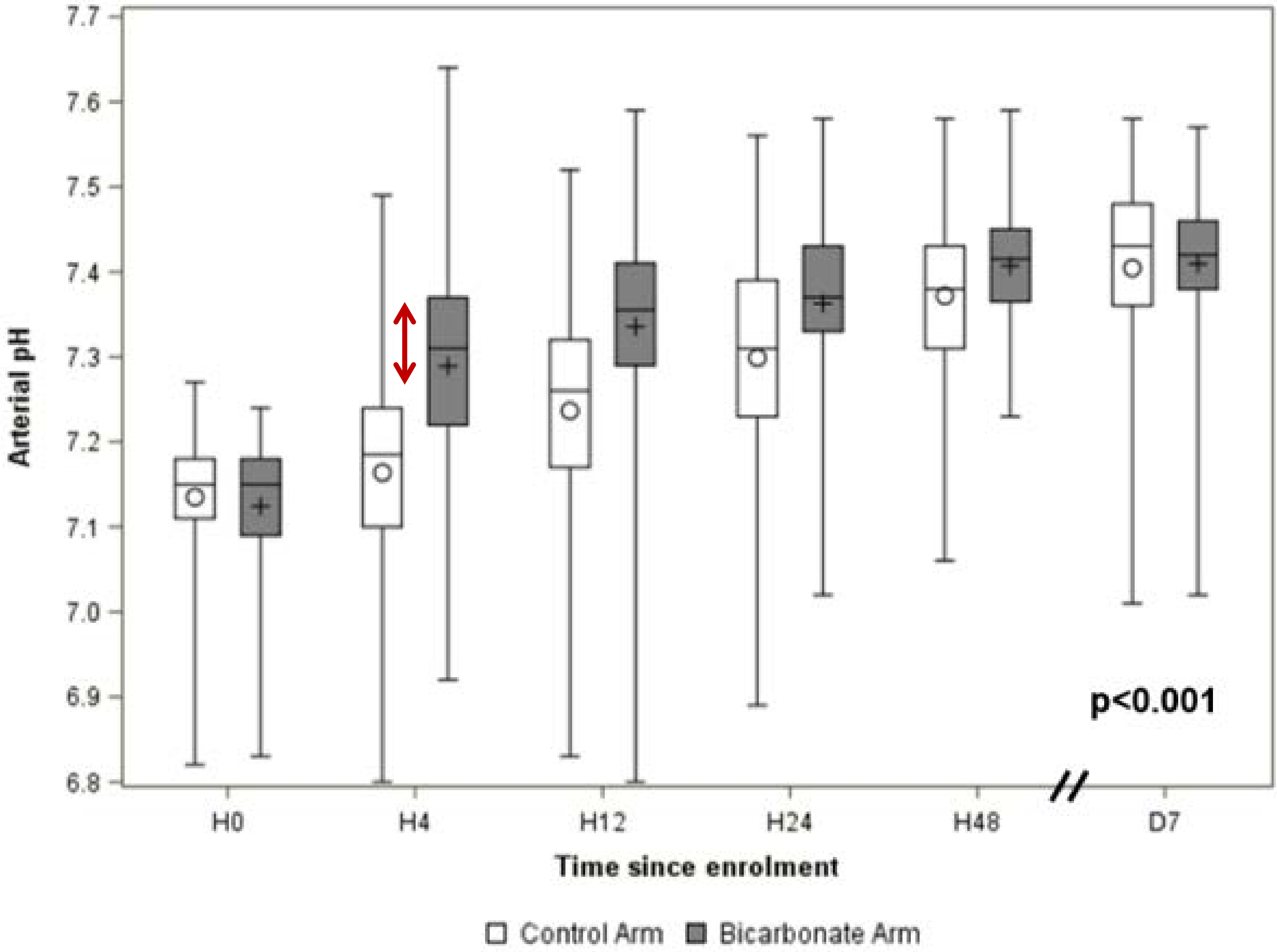

942 patients were assessed for eligibility
542 excluded
109 already received sodium bicarbonate
87 were in terminal decline
76 had treatment limitation
69 had chronic renal failure
47 had immediate RRT indication
41 had ketoacidosis
37 had digestive loss of sodium bicarbonate
21 were eligible but not enrolled
18 were included in another clinical study
13 had hyperkalaemia with heart signs
13 declined to participate
11 were under guardianship protection
400 were randomly assigned


400 were randomly assigned
201 assigned to control group
199 assigned to bicarbonate group
7 withdrew consent
4 withdrew consent
194 included in 28-day follow-up and the intention-to-treat analysis
195 included in 28-day follow-up and the intention-to-treat analysis
22* violated inclusion or non-inclusion criteria
15 violated inclusion or non-inclusion criteria
*
47* received sodium bicarbonate
41 salvage therapies
6 misinterpretations of the protocol
1 did not receive sodium bicarbonate (misinterpretations of the protocol)
132 included in the per-protocol
179 included in the per-protocol

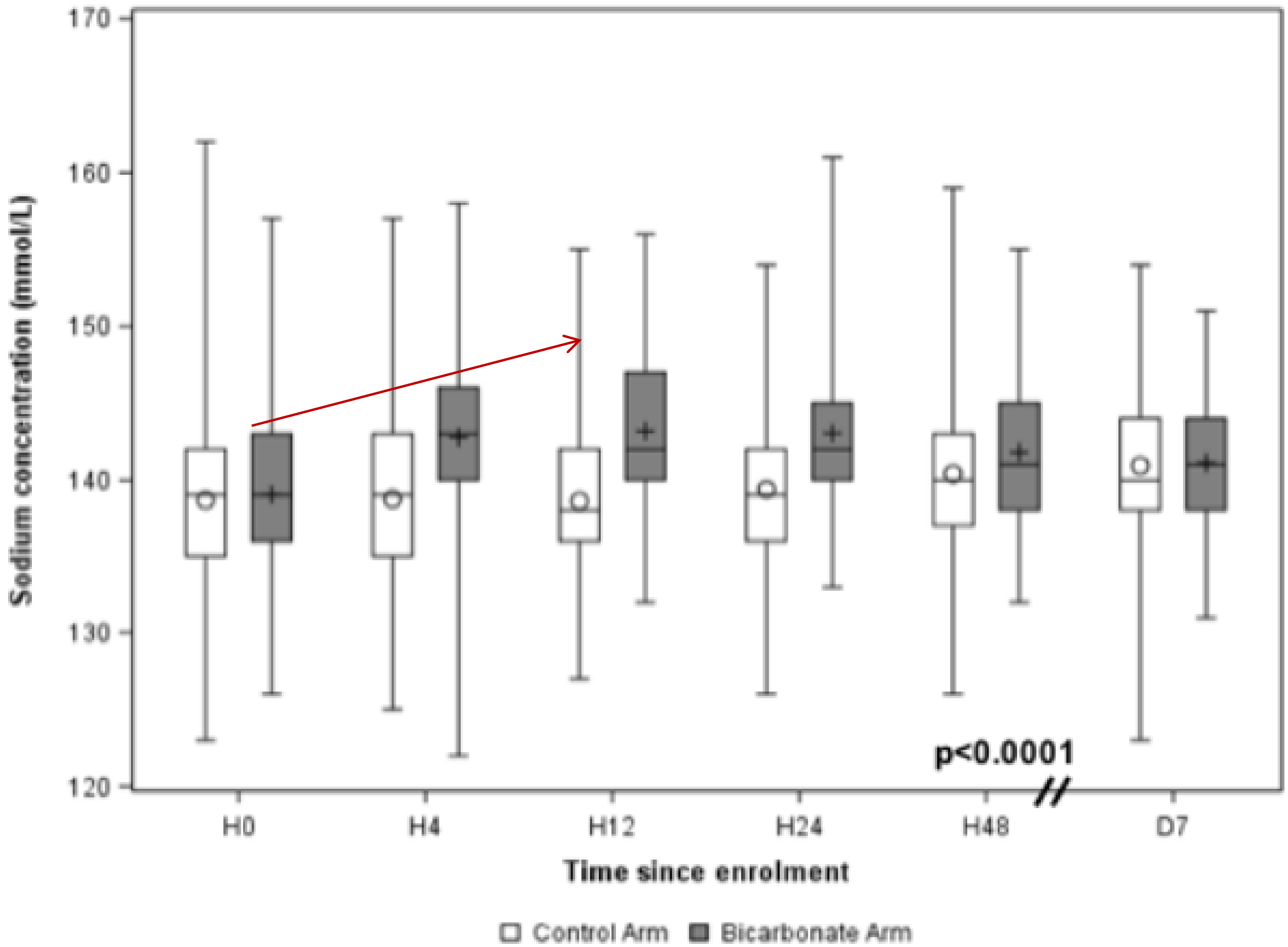
Other secondary outcomes	Control	Bicarb
Overall population (n=389)		
Cumulative fluid intake from enrolment to 24 h (mL)	3500 (1500–5250)	3350 (1800–5250)
Cumulative sodium bicarbonate volume intake from enrolment to 24 h (mL)	0 (0–0)	500 (250–750)
Cumulative sodium bicarbonate intake from enrolment to 24 h (mmol)	0 (0–0)	250 (1255–375)
Cumulative fluid intake from 24 h to 48 h (mL)	1050 (0–2000)	1000 (0–2250)

Total Fluid 48h:	4550	4350
Na mmol/l	130	194
Cl	110	91
K	4	3.3
Est SID	24	~ 100

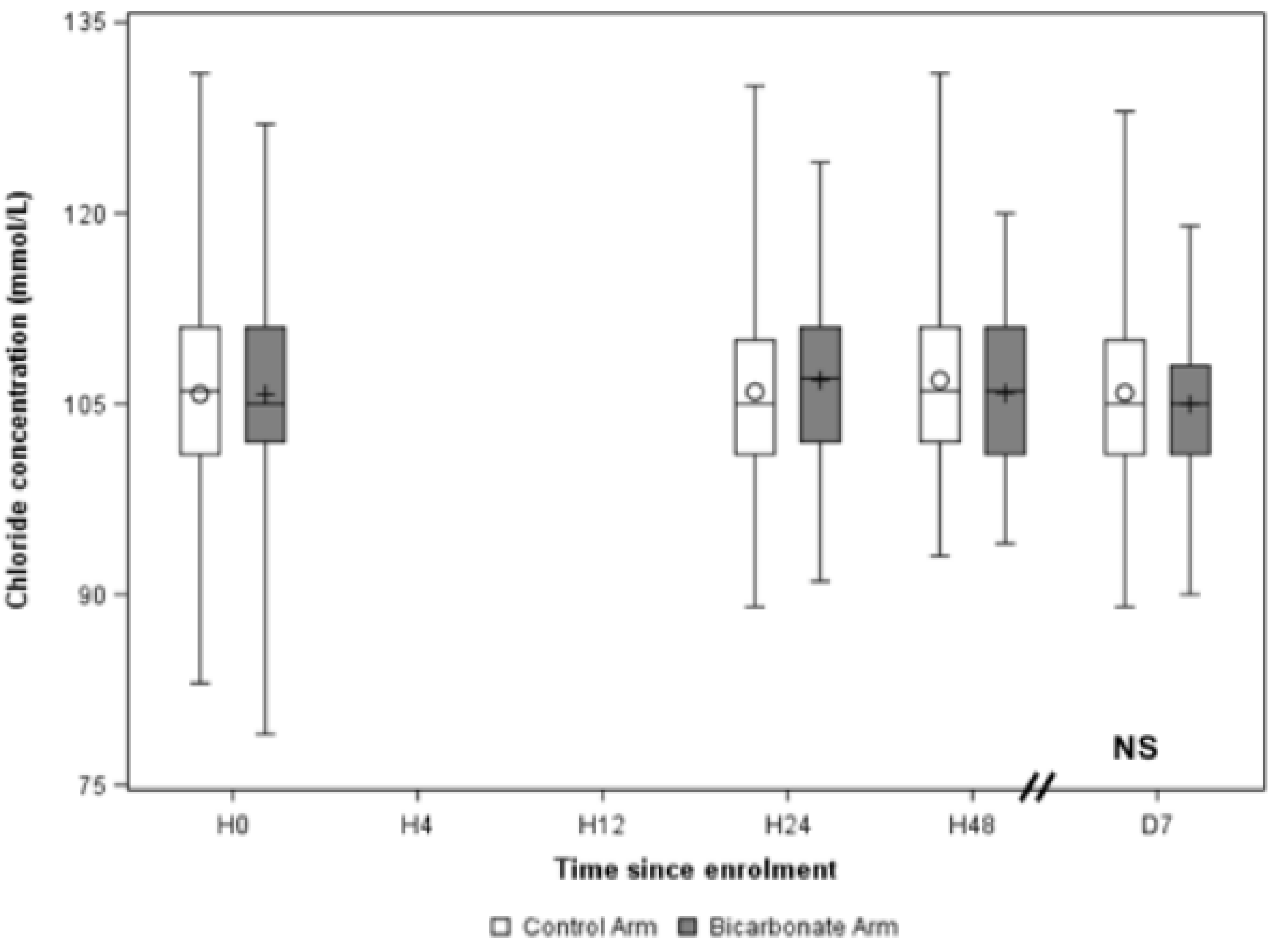
So, what happened to pH?



You can guess what happened to Na

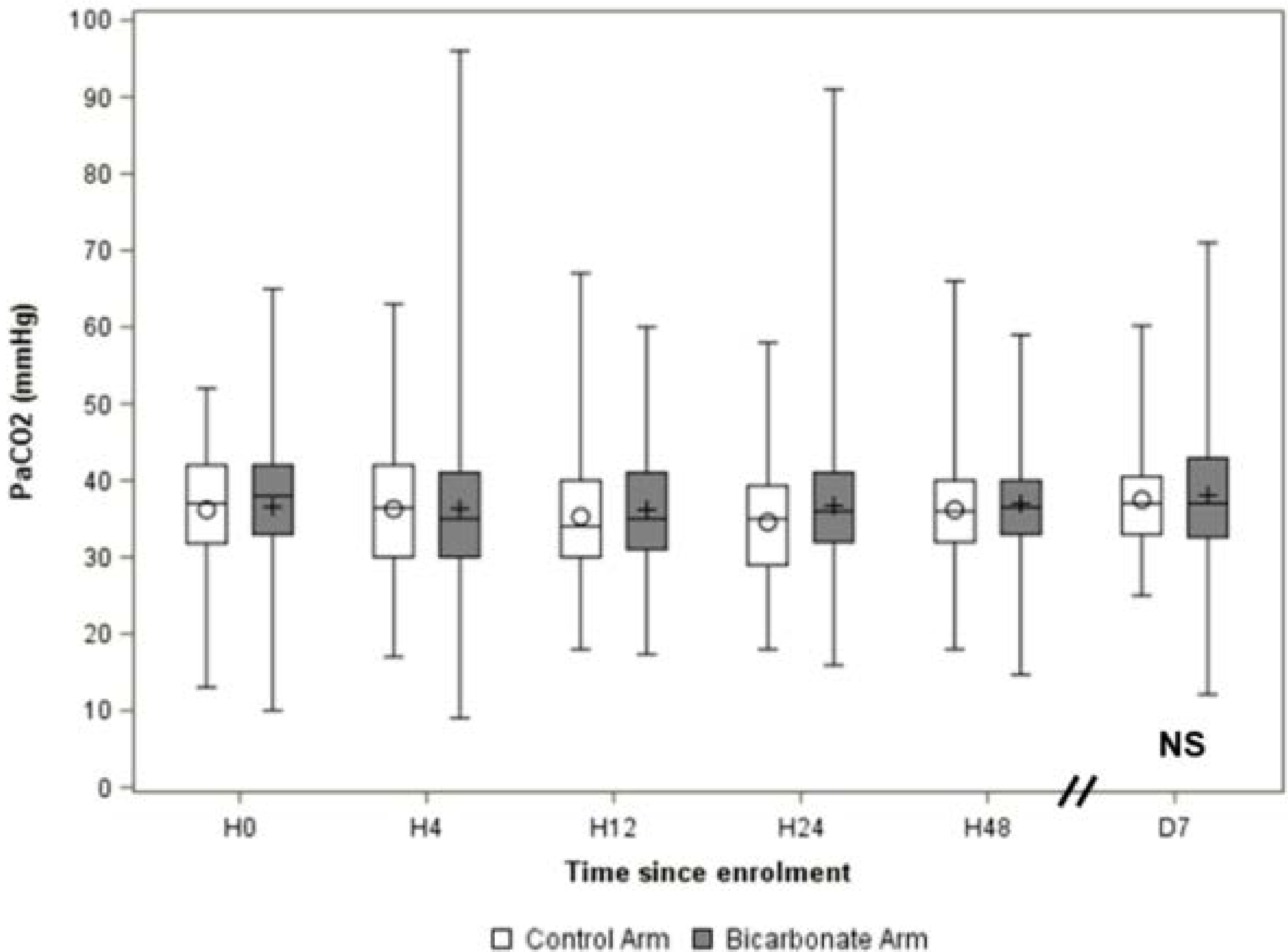


Chloride

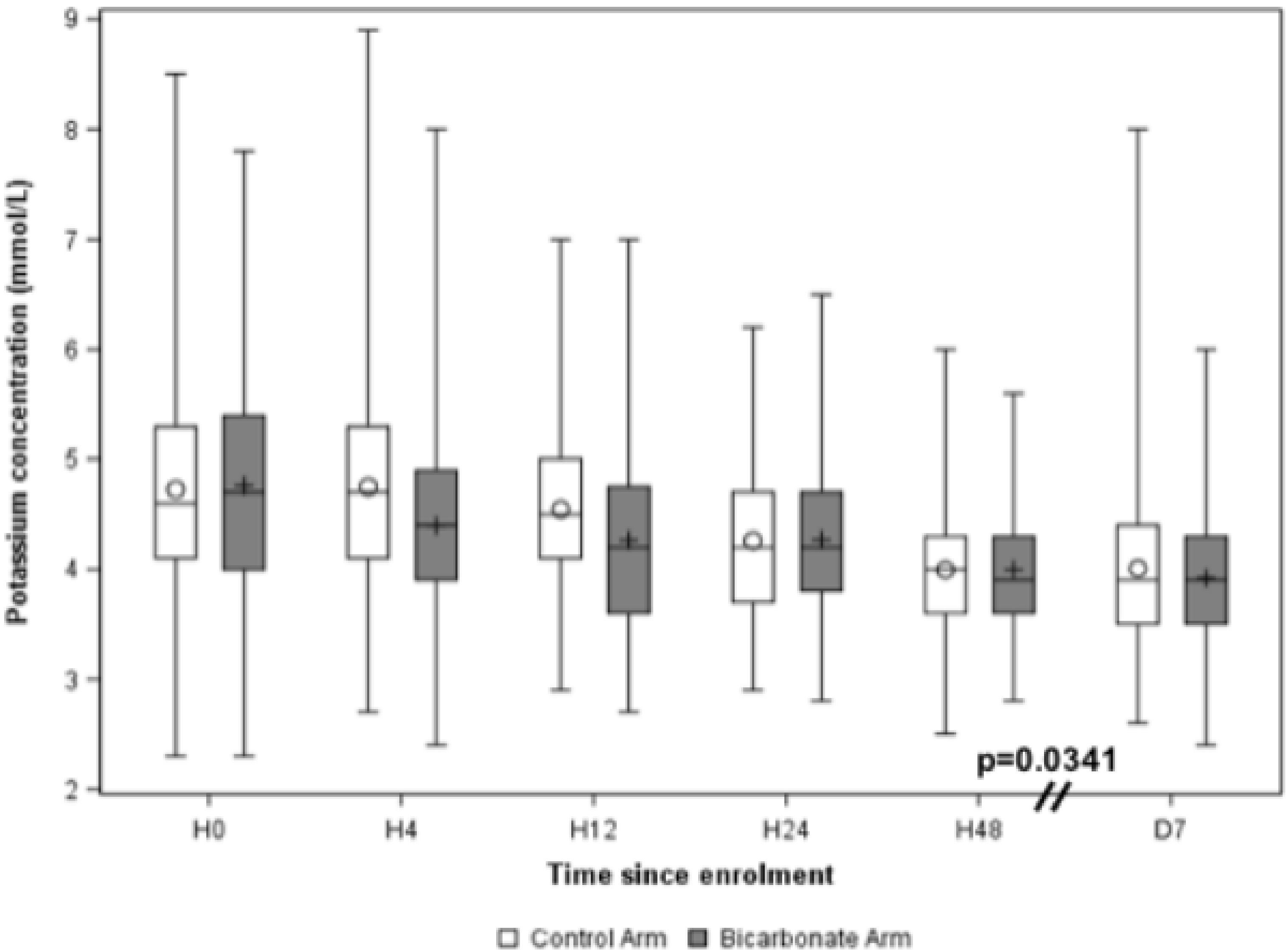


Chloride concentration (mmol/L)
135
120
105
90
75
H0
H4
H12
H24
H48
D7
NS
Time since enrolment
Control Arm
Bicarbonate Arm

What about PaC02 component?



Benefits of this strategy

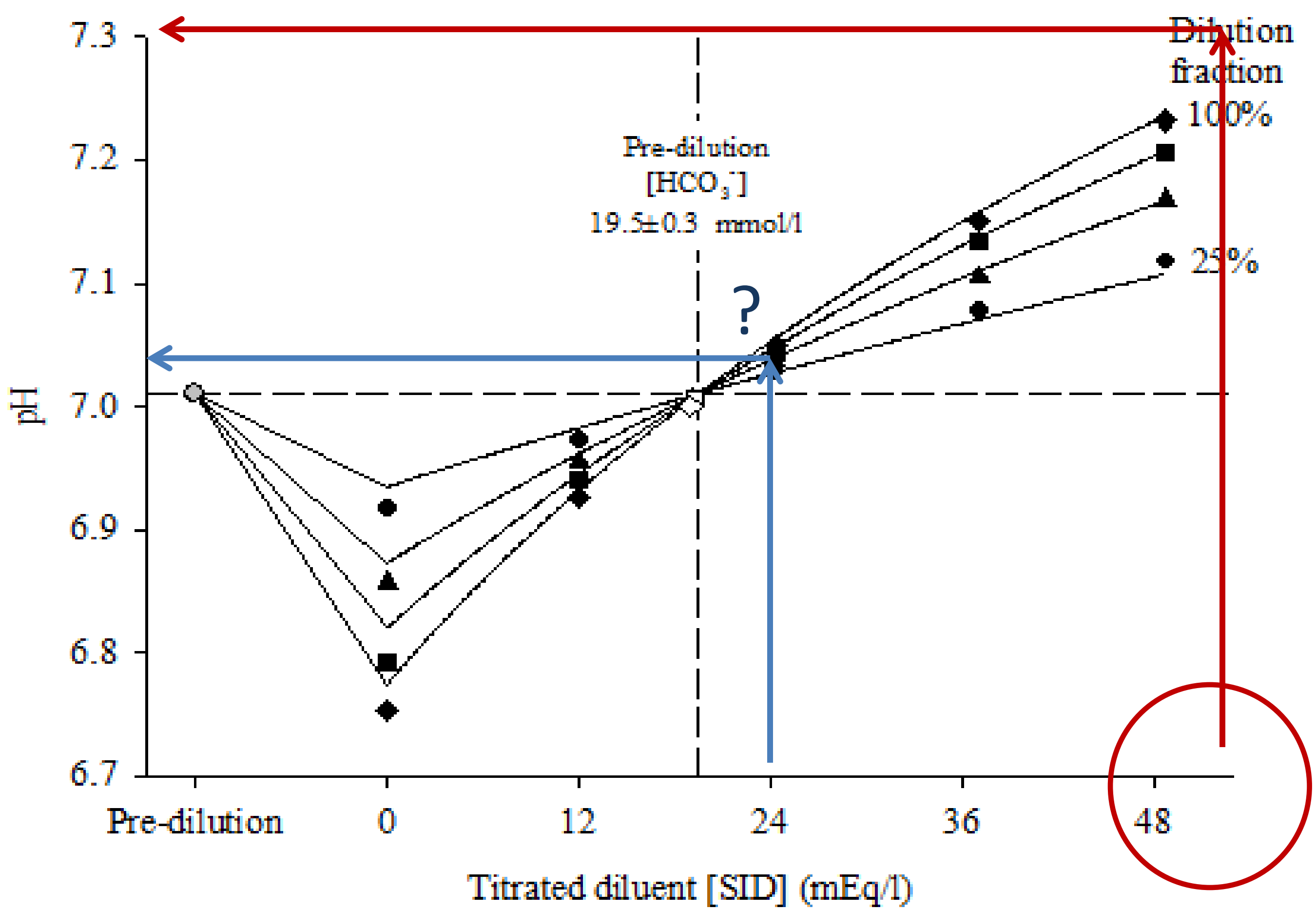


Secondary outcomes			
Renal replacement therapy			
Overall population (n=389)			
Use of renal replacement therapy during ICU stay	100 (52%)	*	68 (35%)
Time from enrolment to initiation of renal replacement therapy (h)	7 (3–18)	*	19 (7–82)
Renal replacement therapy-free days during ICU stay	8 (0–28)	*	19 (1–28)
Renal replacement therapy-free days during ICU stay in survivors	28 (25–28)		28 (25–28)
Dependence on dialysis at ICU discharge	11/32 (34%)		7/32 (22%)
Patients with AKIN scores of 2–3* (n=182)			
Use of renal replacement therapy during ICU stay	66/90 (73%)	*	47/92 (51%)
Time from enrolment to initiation of renal replacement therapy (h)	7 (3–17)	*	20 (8–82)
Renal replacement therapy-free days during ICU stay	1 (0–22)	*	10 (1–28)
Renal replacement therapy-free days during ICU stay in survivors	24 (22–28)		28 (19–28)
Dependence on dialysis at ICU discharge	10/21 (48%)	*	5/25 (20%)

	Control group (n=194)	Bicarbonate group (n=195)	
Primary outcome			Sig p
Overall population (n=389)			
Composite outcome	138 (71%)	128 (66%)	
Day 28 mortality	104 (54%)	87 (45%)	
At least one organ failure at day 7	134 (69%)	121 (62%)	
Patients with AKIN scores of 2–3* (n=182)			
Composite outcome	74/90 (82%)	64/92 (70%)	0.0462
Day 28 mortality	57/90 (63%)	42/92 (46%)	0.0166
At least one organ failure at day 7	74/90 (82%)	61/92 (66%)	0.0142

So back to our question - what you want?

Is this our target?



	Control group (n=194)	Bicarbonate group (n=195)
Age		
Median age (years)	65 (55–75)	66 (55–75)
≥65	100 (52%)	104 (53%)
<65	94 (48%)	104 (47%)
Sex		
Men	123 (63%)	115 (59%)
Women	71 (37%)	80 (41%)
Body-mass index (kg/m²)	27 (23–30)	26 (23–29)
Simplified Acute Physiology Score II*	60 (48–73)	59 (49–73)
Sepsis	115 (59%)	123 (63%)
AKIN status¶		
AKIN 0–1	104 (54%)	103 (53%)
AKIN 2–3	90 (46%)	92 (47%)

	Control group (n=194)	Bicarbonate group (n=195)
(Continued from previous page)		
Physiological support†		
Invasive mechanical ventilation	160 (82%)	164 (84%)
Vasopressor support	156 (80%)	154 (79%)
Laboratory results		
Arterial pH	7·15 (7·11–7·18)	7·15 (7·09–7·18)
PaO_2-to-FiO_2 ratio (mm Hg)	229 (142–355)	264 (144–403)
$PaCO_2$ (mm Hg)	37 (32–42)	38 (33–42)
Serum bicarbonate (mmol/L)	13 (10–15)	13 (10–15)
Serum lactate (mmol/L)	5·3 (3·4–9·0)	6·3 (3·6–9·7)
Serum lactate ≥2 mmol/L at enrolment	152 (78%)	168 (86%)
Serum creatinine (mg/dL)	1·76 (1·21–2·48)	1·67 (1·11–2·33)

What does the data indicate?

Systematic review

Meta-analysis of high- *versus* low-chloride content in perioperative and critical care fluid resuscitation

M. L. Krajewski[1], K. Raghunathan[1,2], S. M. Paluszkiewicz[3], C. R. Schermer[4] and A. D. Shaw[5]

[1]Department of Anesthesiology, Duke University Medical Center, and [2]Anesthesiology Service, Durham VA Medical Center, Durham, North Carolina, [3]Boston Strategic Partners, Boston, Massachusetts, [4]Baxter Healthcare Corporation, Deerfield, Illinois, and [5]Department of Anesthesiology, Vanderbilt University Medical Center, Nashville, Tennessee, USA

Correspondence to: Professor A. D. Shaw, Division of Cardiothoracic Anesthesiology, Vanderbilt University Medical Center, Nashville, Tennessee 37232–8274, USA (e-mail: andrew.shaw@vanderbilt.edu)

2014

Background: The objective of this systematic review and meta-analysis was to assess the relationship between the chloride content of intravenous resuscitation fluids and patient outcomes in the perioperative or intensive care setting.

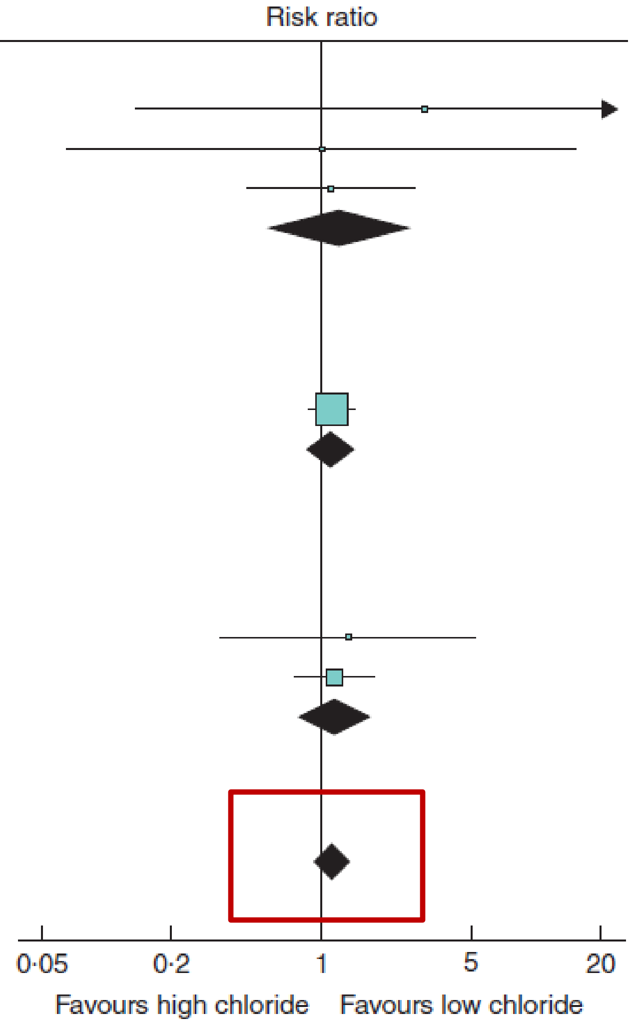
21 studies (6253 pt)

15 RCT, 5 Observational and 1 controlled clinical trial

Mortality

Reference	Mortality: High-chloride	Mortality: Low-chloride	Weight (%)	Risk ratio
RCTs				
Mahajan *et al.*[47]	1 of 11	0 of 11	0·3	3·00 (0·14, 66·53)
Waters *et al.*[14]	1 of 33	1 of 33	0·7	1·00 (0·07, 15·33)
Young *et al.*[54]	8 of 33	7 of 32	4·6	1·11 (0·45, 2·70)
Subtotal	10 of 77	8 of 76	5·6	1·21 (0·53, 2·72)
Heterogeneity: $\chi^2 = 0{\cdot}38$, 2 d.f., $P = 0{\cdot}82$; $I^2 = 0\%$				
Test for overall effect: $Z = 0{\cdot}45$, $P = 0{\cdot}65$				
CCTs				
Yunos *et al.*[26,55]	112 of 760	102 of 773	66·0	1·12 (0·87, 1·43)
Subtotal	112 of 760	102 of 773	66·0	1·12 (0·87, 1·43)
Heterogeneity: not applicable				
Test for overall effect: $Z = 0{\cdot}87$, $P = 0{\cdot}38$				
Observational/retrospective studies				
Berger *et al.*[41]	4 of 20	3 of 20	2·0	1·33 (0·34, 5·21)
Shaw *et al.*[27]	93 of 2778	27 of 926	26·4	1·15 (0·75, 1·75)
Subtotal	97 of 2798	30 of 946	28·4	1·16 (0·78, 1·74)
Heterogeneity: $\chi^2 = 0{\cdot}04$, 1 d.f., $P = 0{\cdot}84$; $I^2 = 0\%$				
Test for overall effect: $Z = 0{\cdot}72$, $P = 0{\cdot}47$				
Total	219 of 3635	140 of 1795	100·0	1·13 (0·92, 1·39)

Heterogeneity: $\chi^2 = 0{\cdot}46$, 5 d.f., $P = 0{\cdot}99$; $I^2 = 0\%$
Test for overall effect: $Z = 1{\cdot}20$, $P = 0{\cdot}23$
Test for subgroup differences: $\chi^2 = 0{\cdot}05$, 2 d.f., $P = 0{\cdot}98$; $I^2 = 0\%$



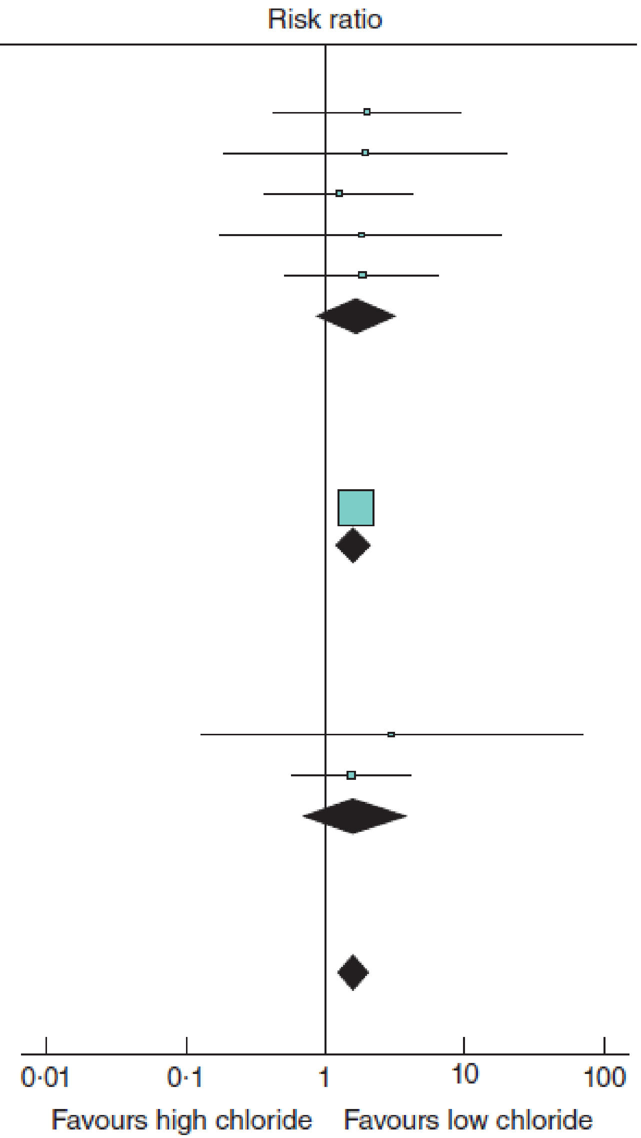
6 studies with mortality as an end point

Reference	AKI/renal failure: High-chloride	AKI/renal failure: Low-chloride	Weight (%)	Risk ratio
RCTs				
Hadimioglu *et al.*[12]	3 of 30	3 of 60	2·4	2·00 (0·43, 9·32)
O'Malley *et al.*[50]	2 of 26	1 of 25	1·2	1·92 (0·19, 19·90)
Waters *et al.*[14]	5 of 33	4 of 33	4·8	1·25 (0·37, 4·25)
Wu *et al.*[53]	2 of 21	1 of 19	1·3	1·81 (0·18, 18·39)
Young *et al.*[54]	6 of 24	3 of 22	3·7	1·83 (0·52, 6·46)
Subtotal	18 of 134	12 of 159	13·4	1·66 (0·83, 3·31)
Heterogeneity: $\chi^2 = 0{\cdot}31$, 4 d.f., $P = 0{\cdot}99$; $I^2 = 0\%$				
Test for overall effect: $Z = 1{\cdot}44$, $P = 0{\cdot}15$				
CCTs				
Yunos *et al.*[26,55]	105 of 760	65 of 773	77·0	1·64 (1·23, 2·20)
Subtotal	105 of 760	65 of 773	77·0	1·64 (1·23, 2·20)
Heterogeneity: not applicable				
Test for overall effect: $Z = 3{\cdot}33$, $P < 0{\cdot}001$				
Observational/retrospective studies				
Berger *et al.*[41]	1 of 20	0 of 20	0·6	3·00 (0·13, 69·52)
Shaw *et al.*[27]	23 of 2778	5 of 926	9·0	1·53 (0·58, 4·02)
Subtotal	24 of 2798	5 of 946	9·6	1·63 (0·65, 4·07)
Heterogeneity: $\chi^2 = 0{\cdot}16$, 1 d.f., $P = 0{\cdot}69$; $I^2 = 0\%$				
Test for overall effect: $Z = 1{\cdot}04$, $P = 0{\cdot}30$				
Total	147 of 3692	82 of 1878	100·0	1·64 (1·27, 2·13)

Heterogeneity: $\chi^2 = 0{\cdot}47$, 7 d.f., $P = 1{\cdot}00$; $I^2 = 0\%$

Test for overall effect: $Z = 3{\cdot}76$, $P < 0{\cdot}001$

Test for subgroup differences: $\chi^2 = 0{\cdot}00$, 2 d.f., $P = 1{\cdot}00$; $I^2 = 0\%$



However,

High Cl fluid:

Other

1. Metabolic acidosis (RR 2.87)
2. Greater serum Cl,
3. More Blood T/F
4. Longer MV

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.,
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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
and the Pragmatic Critical Care Research Group*

2018

Pragmatic, unblinded, Cluster randomized, multiple crossover

Bal vs Saline, % ICU’s in one Center, >15 000 patients

Outcomes

1° - MAKE 30 – Mortality/New RRT/Persistent renal dysfunction

2° Outcomes and Prespecified subgroup analysis

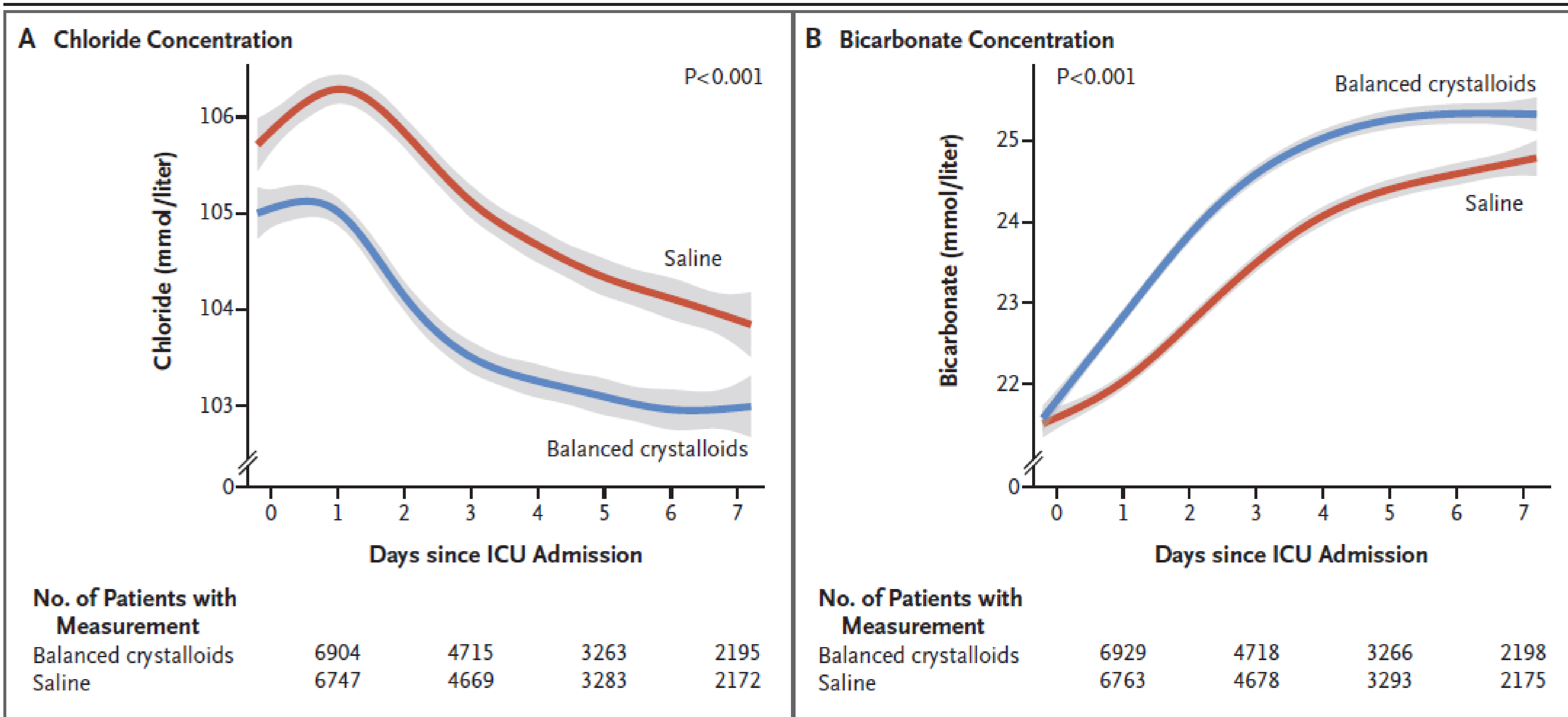
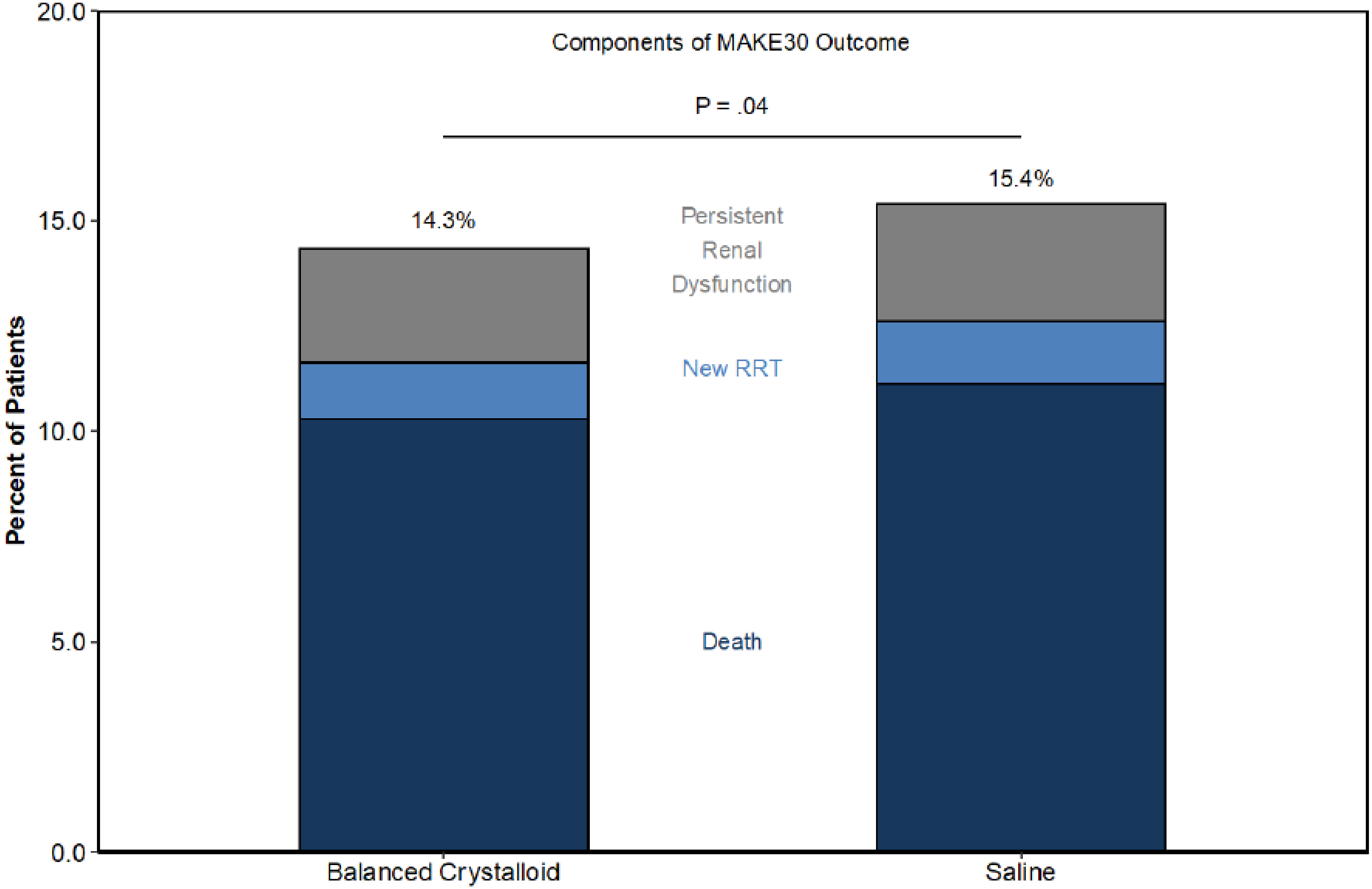


Figure 2. Plasma Chloride and Bicarbonate Concentration According to Group.

Due to co-ordination with ED and OR – Received same fluid pre-ICU, hence the differences at ICU admission

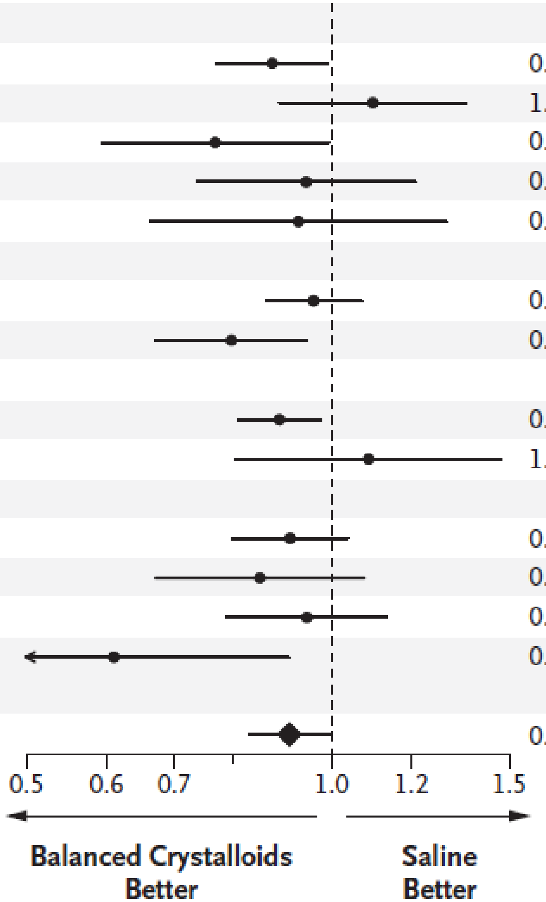
Table 2. Clinical Outcomes.*

Outcome	Balanced Crystalloids (N=7942)	Saline (N=7860)
Primary outcome		
Major adverse kidney event within 30 days — no. (%)‡	1139 (14.3)	1211 (15.4)
Components of primary outcome		
In-hospital death before 30 days — no. (%)	818 (10.3)	875 (11.1)
Receipt of new renal-replacement therapy — no./total no. (%)§	189/7558 (2.5)	220/7458 (2.9)
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)



Components of MAKE30 Outcome
P = .04
14.3%
15.4%
Persistent
Renal
Dysfunction
New RRT
Death
Percent of Patients
20.0
15.0
10.0
5.0
0.0
Balanced Crystalloid
Saline

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
60	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	



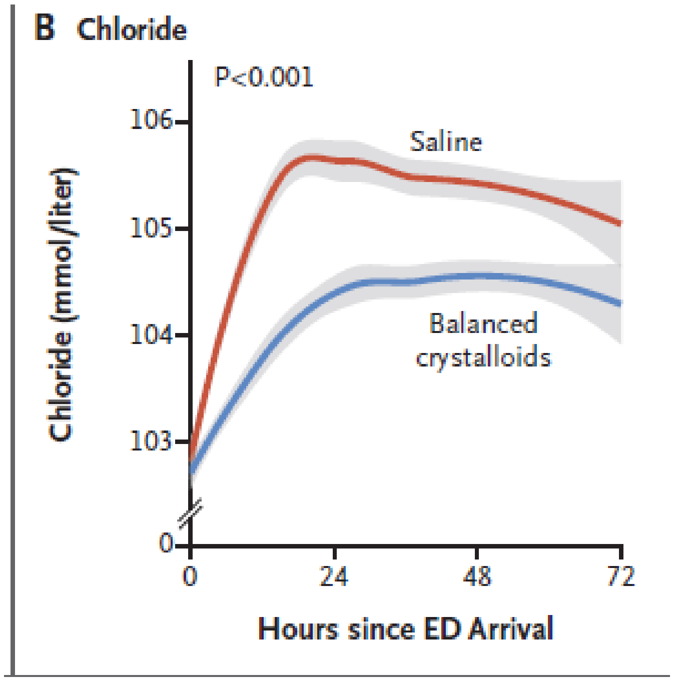
72

The NEW ENGLAND JOURNAL of MEDICINE

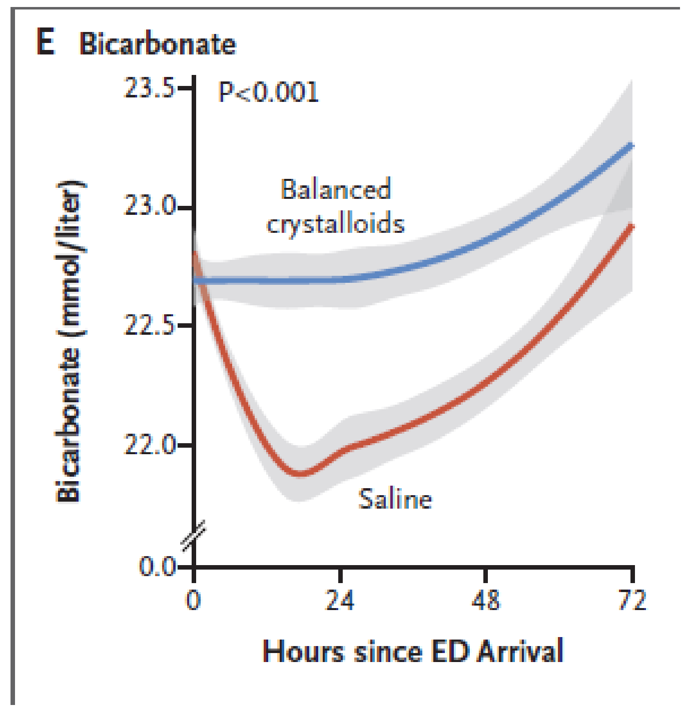
ORIGINAL ARTICLE

Balanced Crystalloids versus Saline in Noncritically Ill Adults

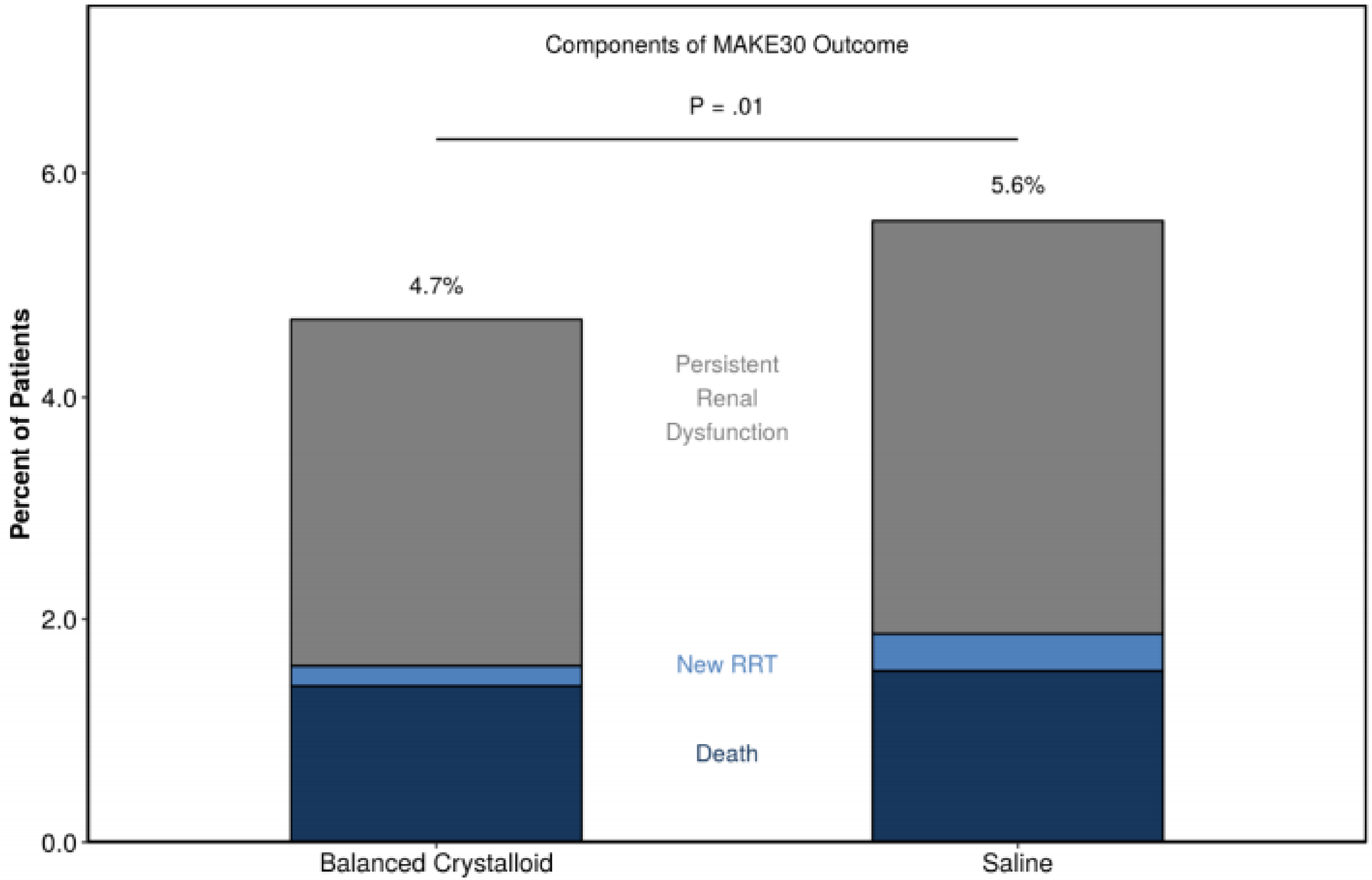
Wesley H. Self, M.D., M.P.H., Matthew W. Semler, M.D.,
Jonathan P. Wanderer, M.D., Li Wang, M.S., Daniel W. Byrne, M.S.,
Sean P. Collins, M.D., Corey M. Slovis, M.D., Christopher J. Lindsell, Ph.D.,
Jesse M. Ehrenfeld, M.D., M.P.H., Edward D. Siew, M.D.,
Andrew D. Shaw, M.B., Gordon R. Bernard, M.D.,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



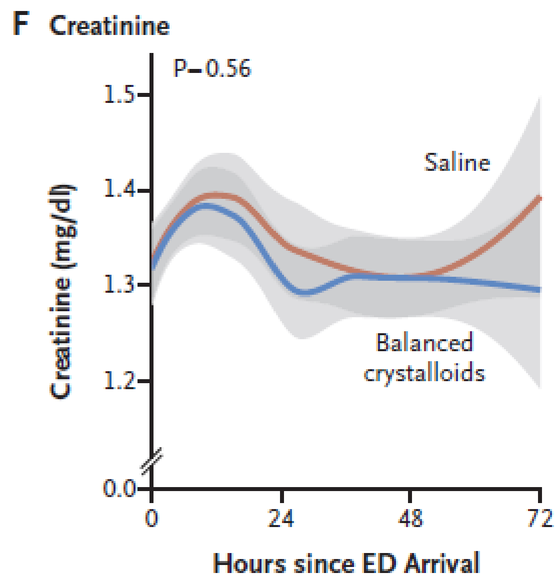
B Chloride
P<0.001
Saline
Balanced crystalloids
Chloride (mmol/liter)
106
105
104
103
0
0
24
48
72
Hours since ED Arrival



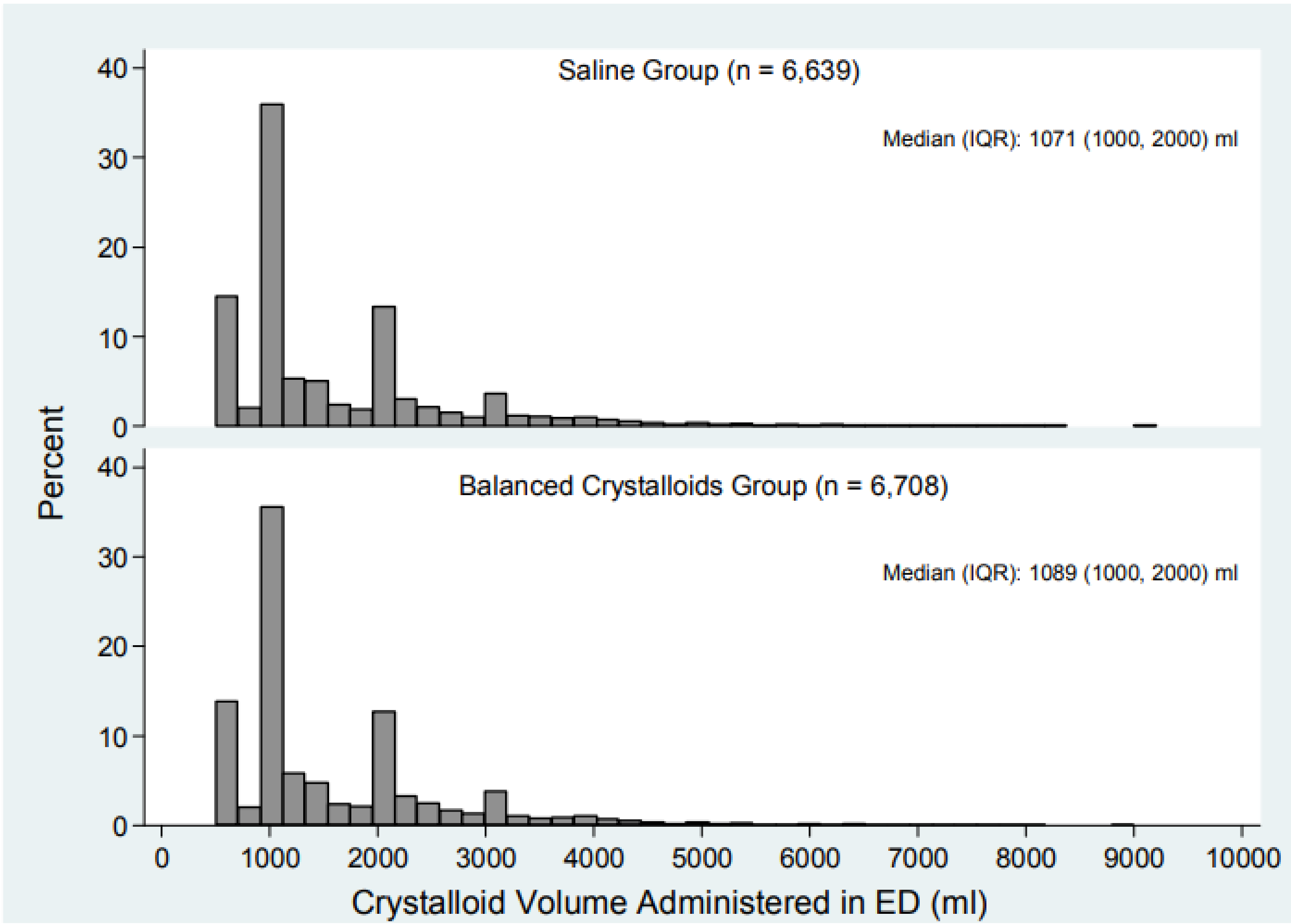
E Bicarbonate
P<0.001
Balanced crystalloids
Saline
Bicarbonate (mmol/liter)
23.5
23.0
22.5
22.0
0.0
0
24
48
72
Hours since ED Arrival



Components of MAKE30 Outcome
P = .01
Percent of Patients
0.0
2.0
4.0
6.0
4.7%
5.6%
Persistent
Renal
Dysfunction
New RRT
Death
Balanced Crystalloid
Saline



F Creatinine
P=0.56
Creatinine (mg/dl)
1.5
1.4
1.3
1.2
0.0
Saline
Balanced
crystalloids
0
24
48
72
Hours since ED Arrival


Saline Group (n = 6,639)
Median (IQR): 1071 (1000, 2000) ml
Balanced Crystalloids Group (n = 6,708)
Median (IQR): 1089 (1000, 2000) ml
Percent
0
10
20
30
40
0
1000
2000
3000
4000
5000
6000
7000
8000
9000
10000
Crystalloid Volume Administered in ED (ml)

Mehta *et al. BMC Nephrology* (2018) 19:91
https://doi.org/10.1186/s12882-018-0876-7

BMC Nephrology

RESEARCH ARTICLE Open Access

The prognostic importance of duration of AKI: a systematic review and meta-analysis

Swati Mehta[1*], Kinsuk Chauhan[2], Achint Patel[2], Shanti Patel[2], Rachel Pinotti[2], Girish N. Nadkarni[2], Chirag R. Parikh[3] and Steven G. Coca[2]

- Duration of AKI was dependent on recovery sCr to within 25-50% of baseline sCr

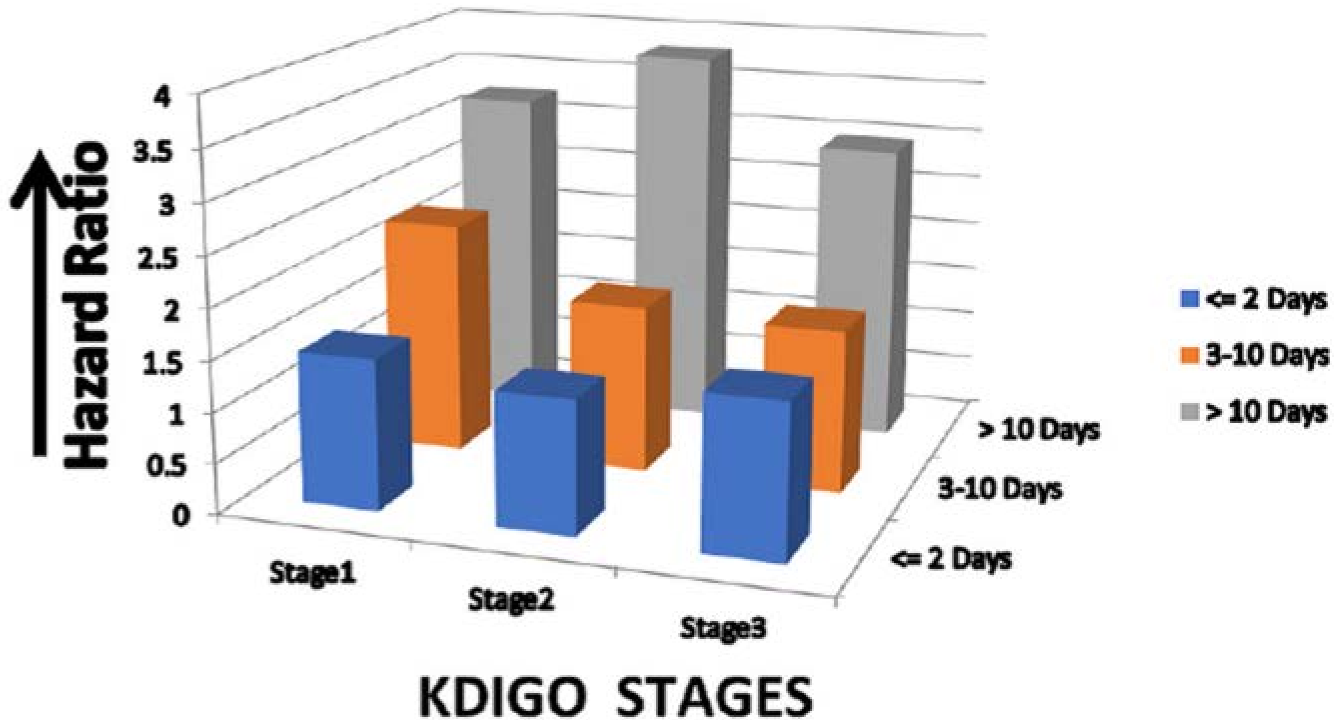


Fig. 5 Risk for incident CKD stage 3 increases with duration even after adjusting for KDIGO stage

Mehta S, Chauhan K, Patel A, Patel S, Pinotti R, Nadkarni GN, et al. The prognostic importance of duration of AKI: a systematic review and meta-analysis. BMC Nephrol [Internet]. 2018 Apr 19;19. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5907696/

Conclusion

- Duration of AKI is independently associated with long-term mortality and may provide additional prognostic information over and above magnitude of serum creatinine alone. Thus, AKI duration can be considered as a prognostic factor for long-term mortality and other cardiovascular outcomes and can be used as an endpoint in intervention trials to prevent or treat AKI.

Mehta S, Chauhan K, Patel A, Patel S, Pinotti R, Nadkarni GN, et al. The prognostic importance of duration of AKI: a systematic review and meta-analysis. BMC Nephrol [Internet]. 2018 Apr 19;19. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5907696/

What about SPLIT

eTable 7. Cause-specific in hospital mortality within the 90-day follow-up period

	Buffered crystalloid group	Saline group	Relative Risk (95% CI)	P value
Categories – no. / total no. (%)				
Bleeding	3/1152 (0.3)	2/1110 (0.2)	1.45 (0.24 to 8.63)	1.00
Cardiac	14/1152 (1.2)	20/1110 (1.8)	0.67 (0.34 to 1.33)	0.30
Cerebral	32/1152 (2.8)	39/1110 (3.5)	0.79 (0.5 to 1.25)	0.34
Sepsis	30/1152 (2.6)	23/1110 (2.1)	1.26 (0.73 to 2.15)	0.41
Other	8/1152 (0.7)	11/1110 (1)	0.7 (0.28 to 1.74)	0.50
Total	87/1152 7.6%	95/1110 8.6%		

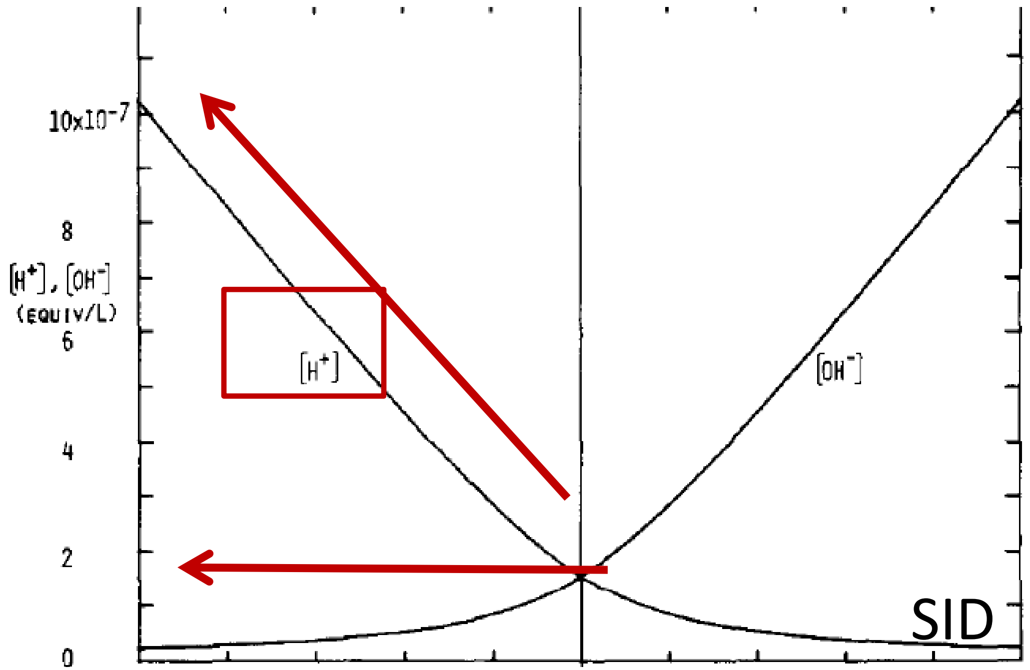
1% absolute mortality reduction – obviously not significant

Young et al. JAMA 2015

dissolved CO_2, H_2CO_3, HCO_3^-, and CO_3^{2-}. Our three laws permit us to write eight simultaneous equations involving these components:

Water dissociation equilibrium:	$[H^+] \times [OH^-] = K'w$
Weak acid dissociation equilibrium:	$[H^+] \times [A^-] = K_A \times [HA]$
Weak acid conservation of mass:	$[HA] + [A^-] = [A_{TOT}]$
CO_2 solution equilibrium:	$[CO_2\,(dslvd)] = S_{CO_2} \times P_{CO_2}$
Carbonic acid equilibrium:	$[H_2CO_3] = S_{H_2CO_3} \times P_{CO_2}$
Bicarbonate equilibrium:	$[H^+] \times [HCO_3^-] = K_C \times P_{CO_2}$
Carbonate equilibrium:	$[H^+] \times [CO_3^{2-}] = K_3 \times [HCO_3^-]$
Electrical neutrality:	$[S.I.D.] + [H^+] - [OH^-] - [A^-] - [HCO_3^-] - [CO_3^{2-}] = 0$

What does a change in Cl^- do?



2. Alb^-
3. PaC02

1. Na^+ $-Cl^-$

$$[H^+] = \sqrt{K'w + ([SID]/2)^2} - ([SID]/2)$$

$$[OH^-] = \sqrt{K'w + ([SID]/2)^2} + ([SID]/2)$$

SMART

Table S11. Indications for new renal replacement therapy.

	Balanced	**Saline**	
Indications for new RRT among patients who received new RRT, No. (%)	**(n = 189)**	**(n = 220)**	***P* value**
Oliguria	144 (76.2)	180 (81.8)	0.16
Hyperkalemia with plasma potassium > 6.5 mEq/L	21 (11.1)	27 (12.3)	0.72
Acidemia with pH < 7.20	56 (29.6)	64 (29.1)	0.91
Blood urea nitrogen > 70 mg/dL	82 (43.4)	106 (48.2)	0.33
Plasma creatinine > 3.39 mg/dL	111 (58.7)	135 (61.4)	0.59
Organ edema	58 (30.7)	66 (30.0)	0.88
Other renal failure–related indication	19 (10.1)	21 (9.5)	0.86
Other non–renal failure–related indication	42 (22.2)	54 (24.5)	0.58