Choc Septique

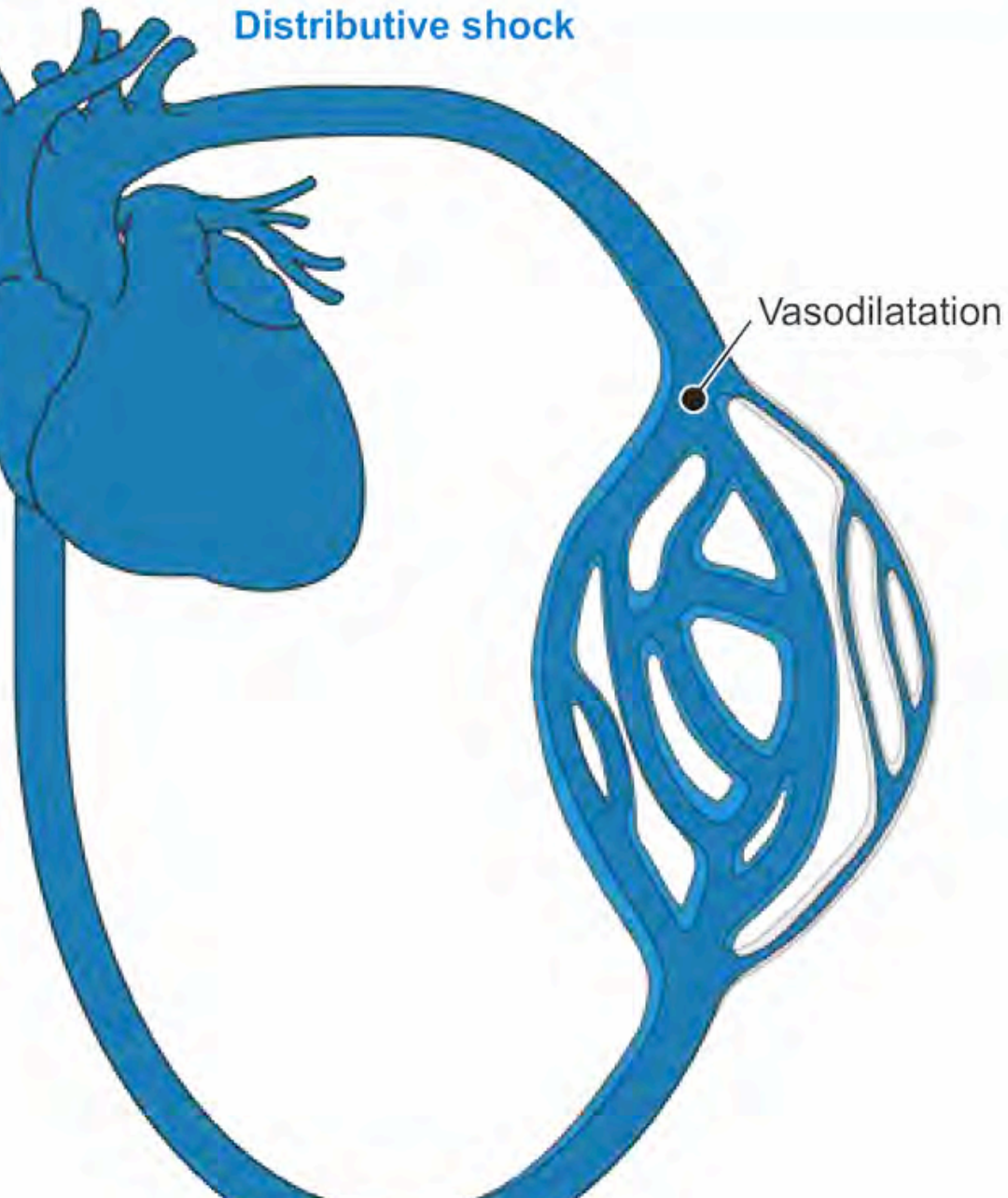
uelle place pour les colloïdes

Pr Jean-Paul Mira
Service de réanimation- Hôpital Cochin – Paris -

Déclare les liens suivants :

- LFB
- Fresénius
- Baxter

Jean-Louis Vincent, M.D., Ph.D., and Daniel De Backer, M.D., Ph.D.



SIGNS OF CIRCULATORY SHOCK PATHWAY

Arterial hypotension and usually tachycardia

↓

Signs of tissue hypoperfusion present

- Altered mental state
- Mottled, clammy skin
- Oliguria
- Elevated blood lactate

↓

Circulatory shock

↓

Normal or high cardiac output or SvO_2

↓

Distributive

SYMPTOMS

Distributive shock is charact
by hypovolemia and hypote
is the result of vasodilatation
release of inflammatory me

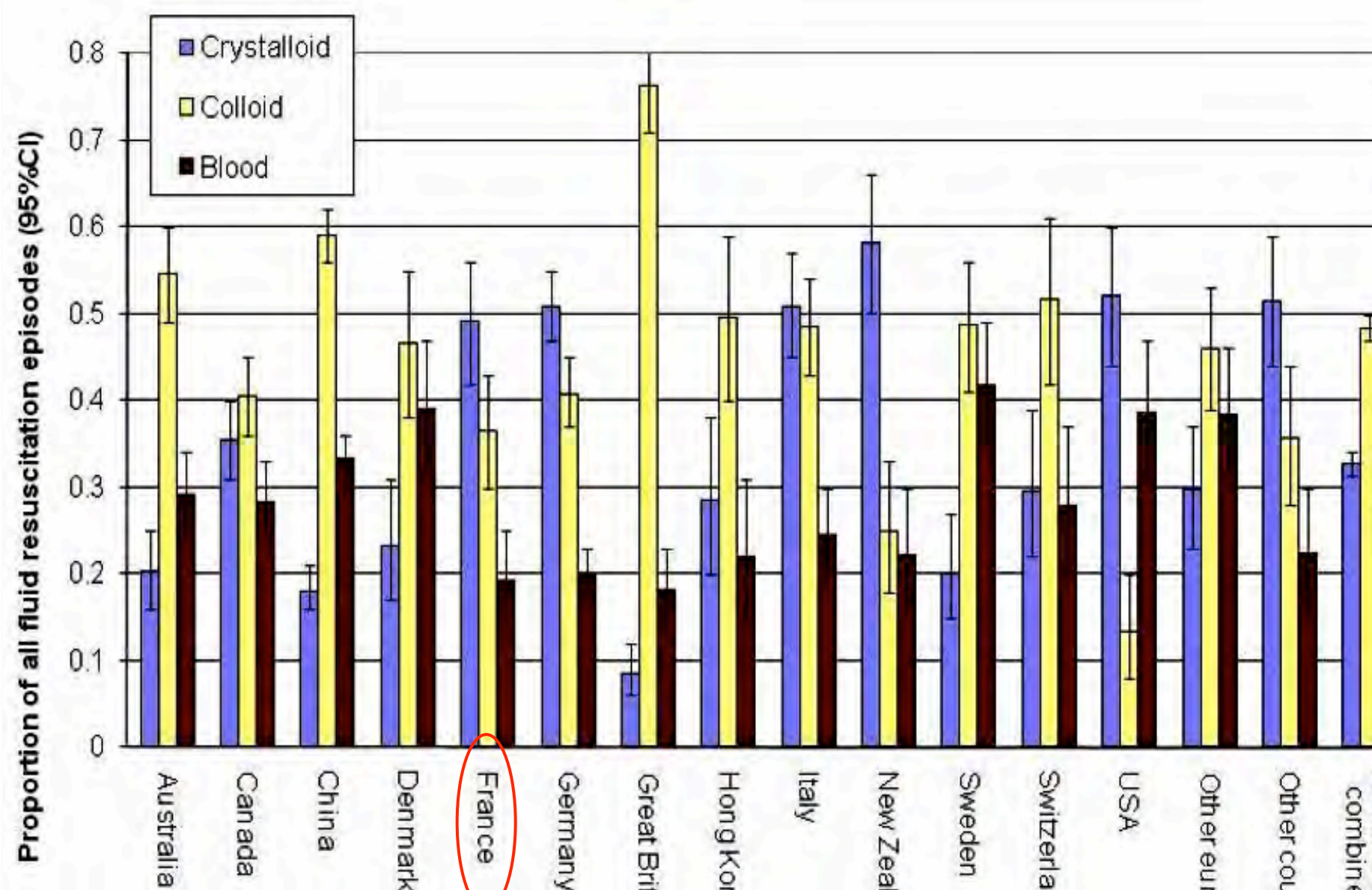
ECHOCARDIOGRAPHIC

Normal cardiac chambers a
(usually) preserved contract

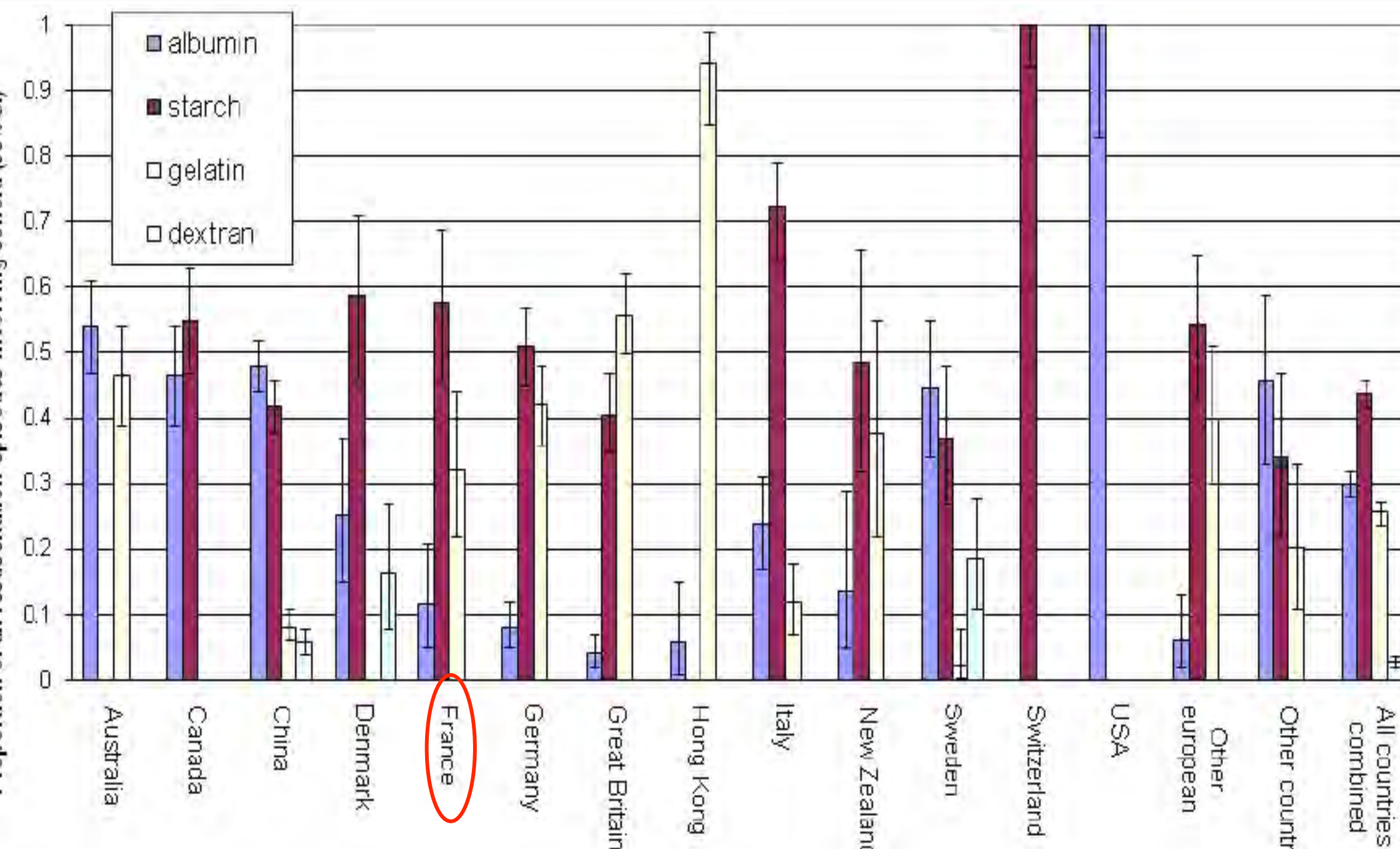
intensive care units

One day observational study 391 ICUs (25 countries)
1955 patients 4488 fluid resuscitation episodes

our study



international cross-sectional study in 391 intensive care units



ABSTRACT

suscitation is an essential aspect of the management of patients with severe sepsis and septic sho
the early stages of disease. Which fluid should be used for this purpose has been a topic of ong
es heated debate for many years, yet this is still little evidence to support one fluid over another. E
specific adverse effects, and all fluids when given in excess can be detrimental. In this article, we wi

Fluid	Adverse effects
IDS (general)	Costs/risks of fluid overload/hyperconcocity-induced renal failure/altered h
	High costs
	Limited efficacy/allergic reactions
	Allergic reactions/altered blood crossmatching, altered hemostasis, renal fail
	Altered hemostasis/long persistence in the body/pruritus/renal failure
LLOIDS (general)	Short-lived hemodynamic effects/electrolyte changes
(%)	Hyperchloremic acidosis
actate	Hypotonicity/lactate load/Ca content
te	Acetate and gluconate load

dies have been conducted with higher MW HES solutions.

pecial Articles

urviving Sepsis Campaign: International uidelines for Management of Severe Sepsis nd Septic Shock: 2012

R. Phillip Dellinger, MD[1]; Mitchell M. Levy, MD[2]; Andrew Rhodes, MB BS[3]; Djillali Annane, MD[4]; Herwig Gerlach, MD, PhD[5]; Steven M. Opal, MD[6]; Jonathan E. Sevransky, MD[7]; Charles L. Sprung, MD Ivor S. Douglas, MD[9]; Roman Jaeschke, MD[10]; Tiffany M. Osborn, MD, MPH[11]; Mark E. Nunnally, MD Sean R. Townsend, MD[13]; Konrad Reinhart, MD[14]; Ruth M. Kleinpell, PhD, RN-CS[15]; Derek C. Angus, MD, MPH[16]; Clifford S. Deutschman, MD, MS[17]; Flavia R. Machado, MD, PhD[18]; Gordon D. Rubenfeld, MD[19]; Steven A. Webb, MB BS, PhD[20]; Richard J. Beale, MB BS[21]; Jean-Louis Vincent, MD, PhD[22]; Rui Moreno, MD, PhD[23]; and the Surviving Sepsis Campaign Guidelines Committee including the Pediatric Subgroup*

We recommend crystalloids as the initial fluid of choice (gra

1B)

We recommend against the use of hydroxyethyl starches (HE

for fluid resuscitation of severe sepsis and septic shock (gra

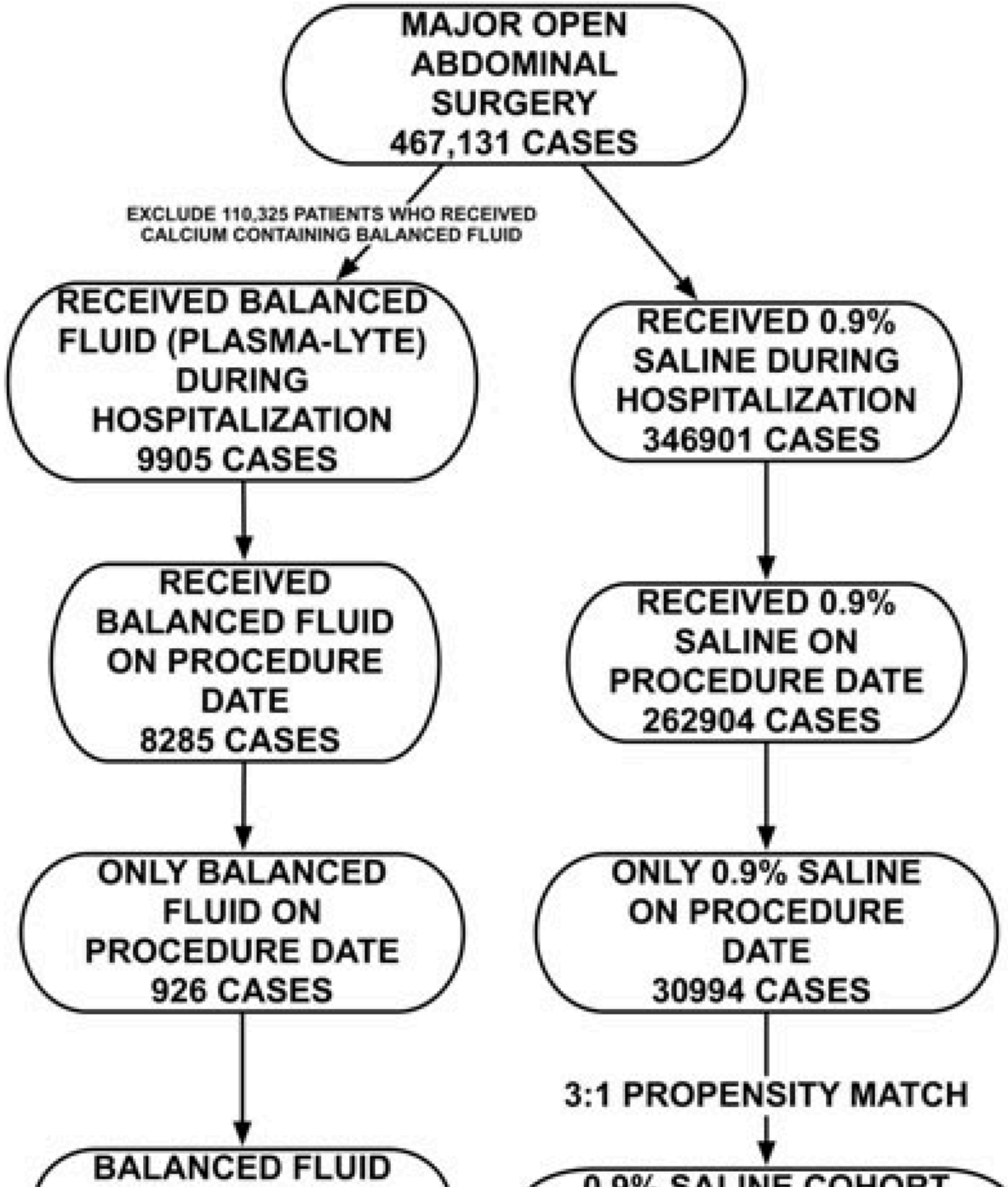
1B)

We suggest the use of albumin in the fluid resuscitation of sev

sepsis and septic shock when patients require substan

amounts of crystalloids (grade 2C).

0.9% Saline Compared to Plasma-Lyte



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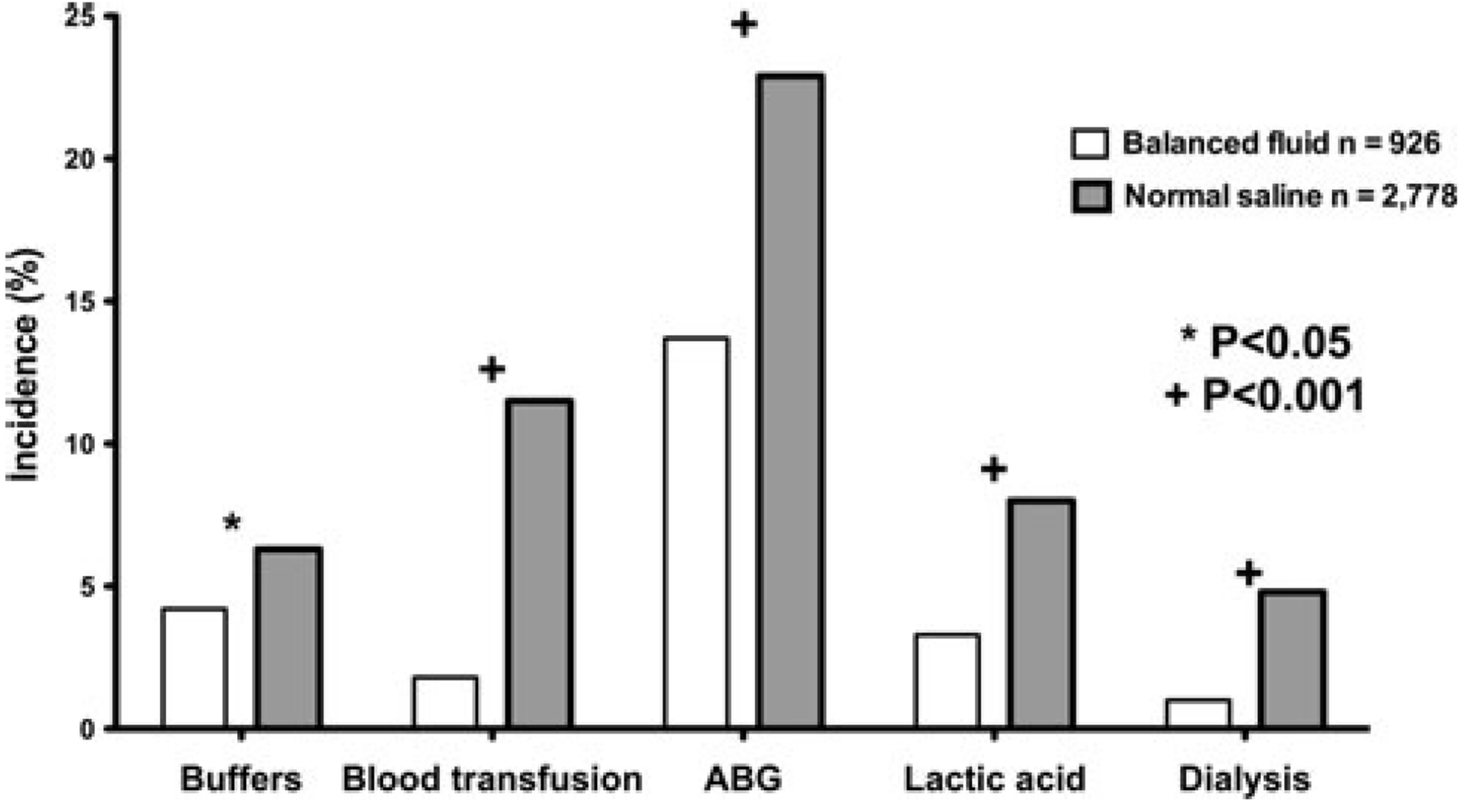


ntravenous 0.9% Saline and General Surgical Patient

A problem, Not a Solution

Dileep N. Lobo, DM, FRCS, FACS

Annals of Surgery • Volume 255, Number 5, May 20

Chloride-Restrictive Intravenous Fluid ministration Strategy and Kidney Injury Critically Ill Adults

Mohd Yunos, MD
Bellomo, MD, FCICM

JAMA. 2012;308:1566

RESEARCH HIGHL

ews Nephrology **8**, 679 (2012); published online 13 November 2012; doi:10.1038/nrneph.2012.221

IDNEY INJURY

striction of intravenous chloride intake may redu

Administration Strategy and Kidney Injury in Critically Ill Adults

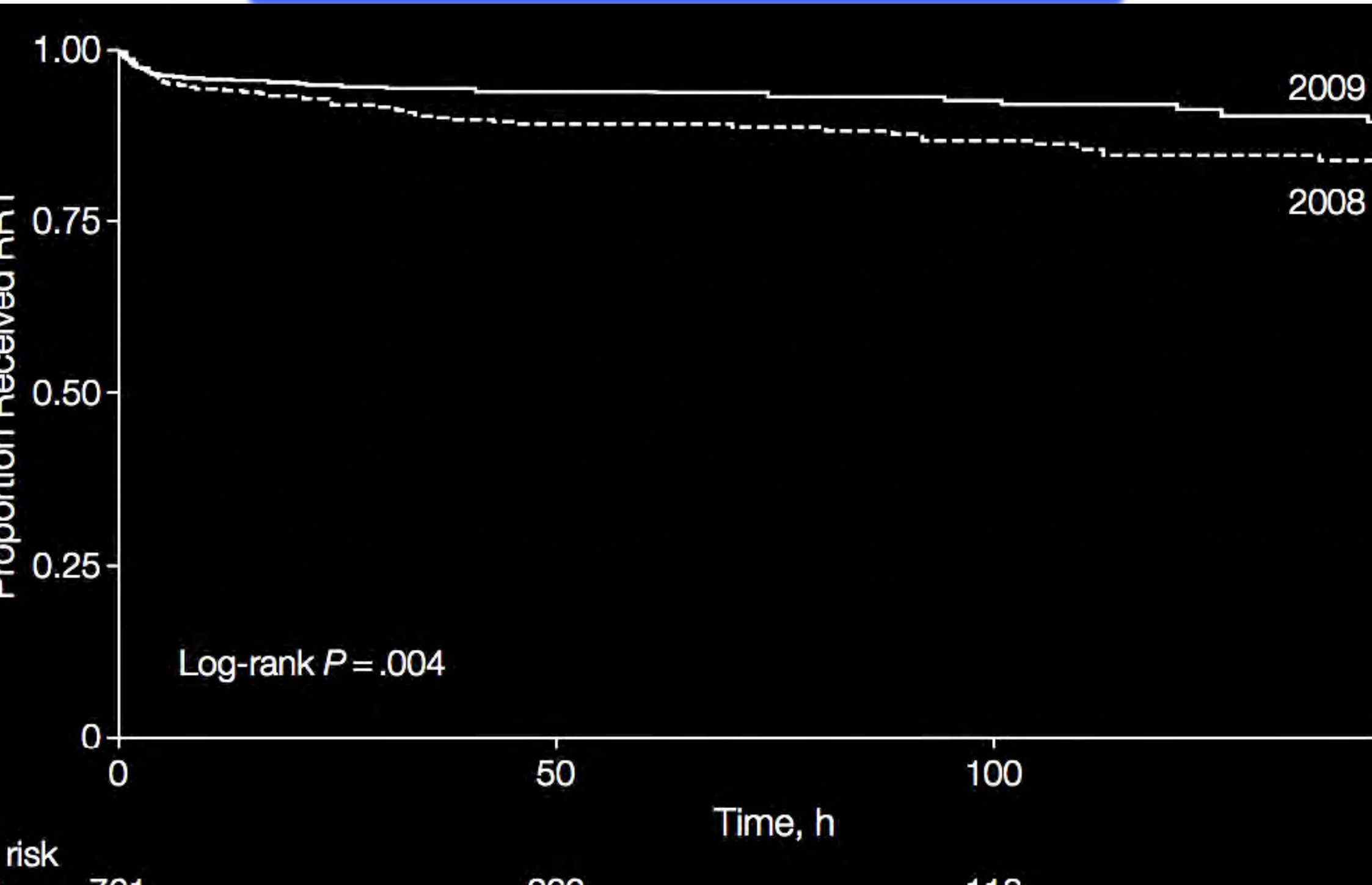
Prospective, open-label, sequential period pilot study

	0.9% Saline	Hartmann	4% Gelatin	Plasma-Lyte 148	Albumin 4%	Albumin 20%
Sodium	150	129	154	140	140	48-100
Potassium	0	5	0	5	0	0
Chloride	150	109	120	98	128	19
Calcium	0	2	0	0	0	0
Magnesium	0	0	0	1.5	0	0
Lactate	0	29	0	0	0	0
Acetate	0	0	0	27	0	0
Gluconate	0	0	0	23	0	0
Octanoate	0	0	0	0	6.4	32

694 mmol/pt

496 mmol/pt

Administration Strategy and Kidney Injury in Critically Ill Adults



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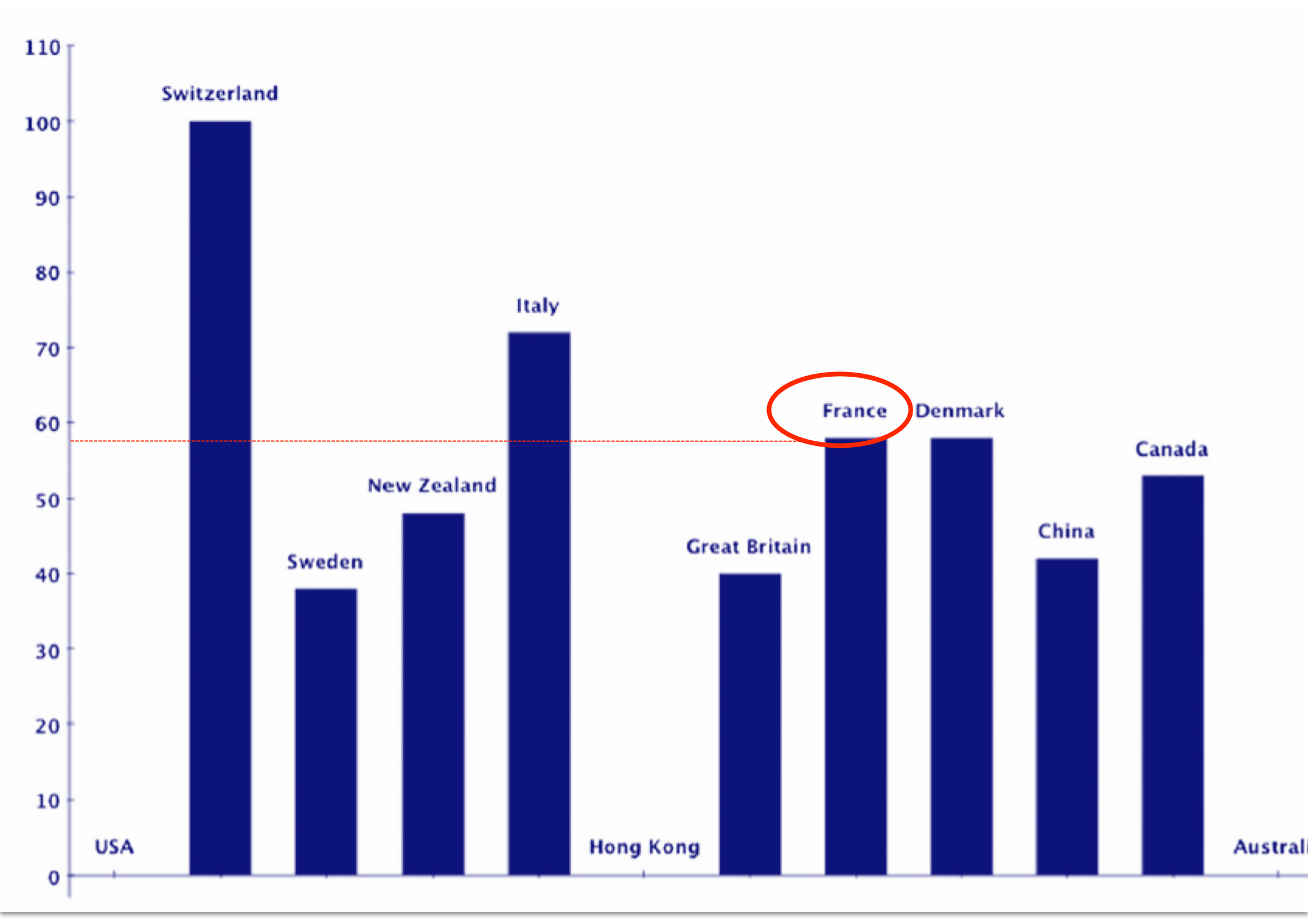
110
100
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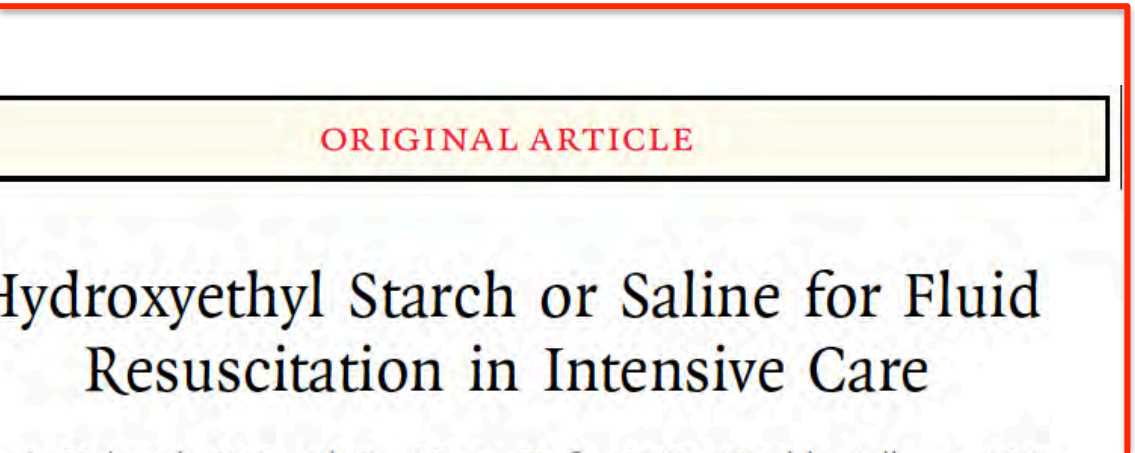
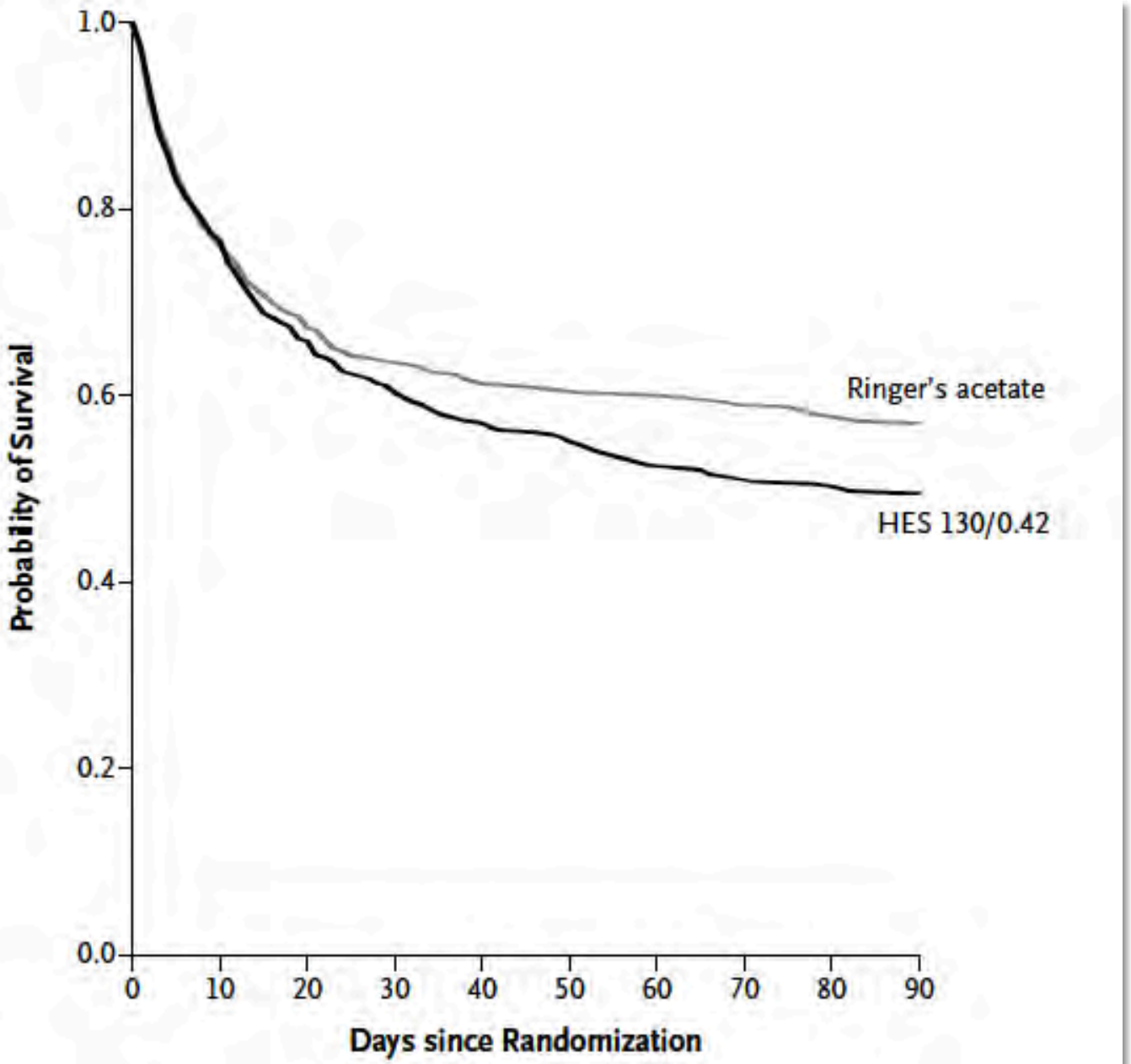
Switzerland
Sweden
New Zealand
Italy
Great Britain
France
Denmark
China
Canada
USA
Hong Kong

sis: a multicentre randomised study

que Schortgen, Jean-Claude Lacherade, Fabrice Bruneel, Isabelle Cattaneo, François Hemery, François Lemaire,
t Brochard

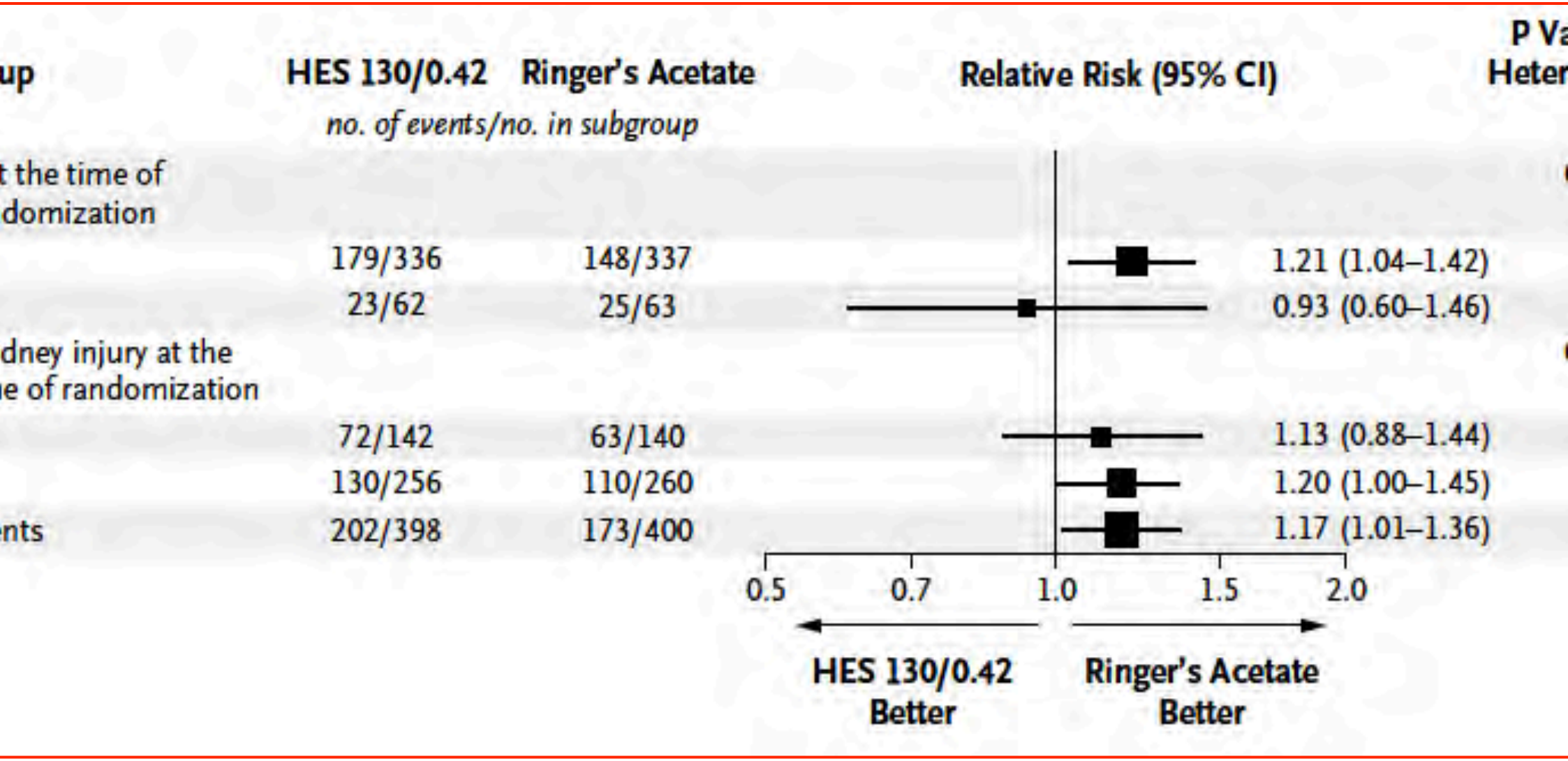


Ringer's Acetate in Severe Sepsis

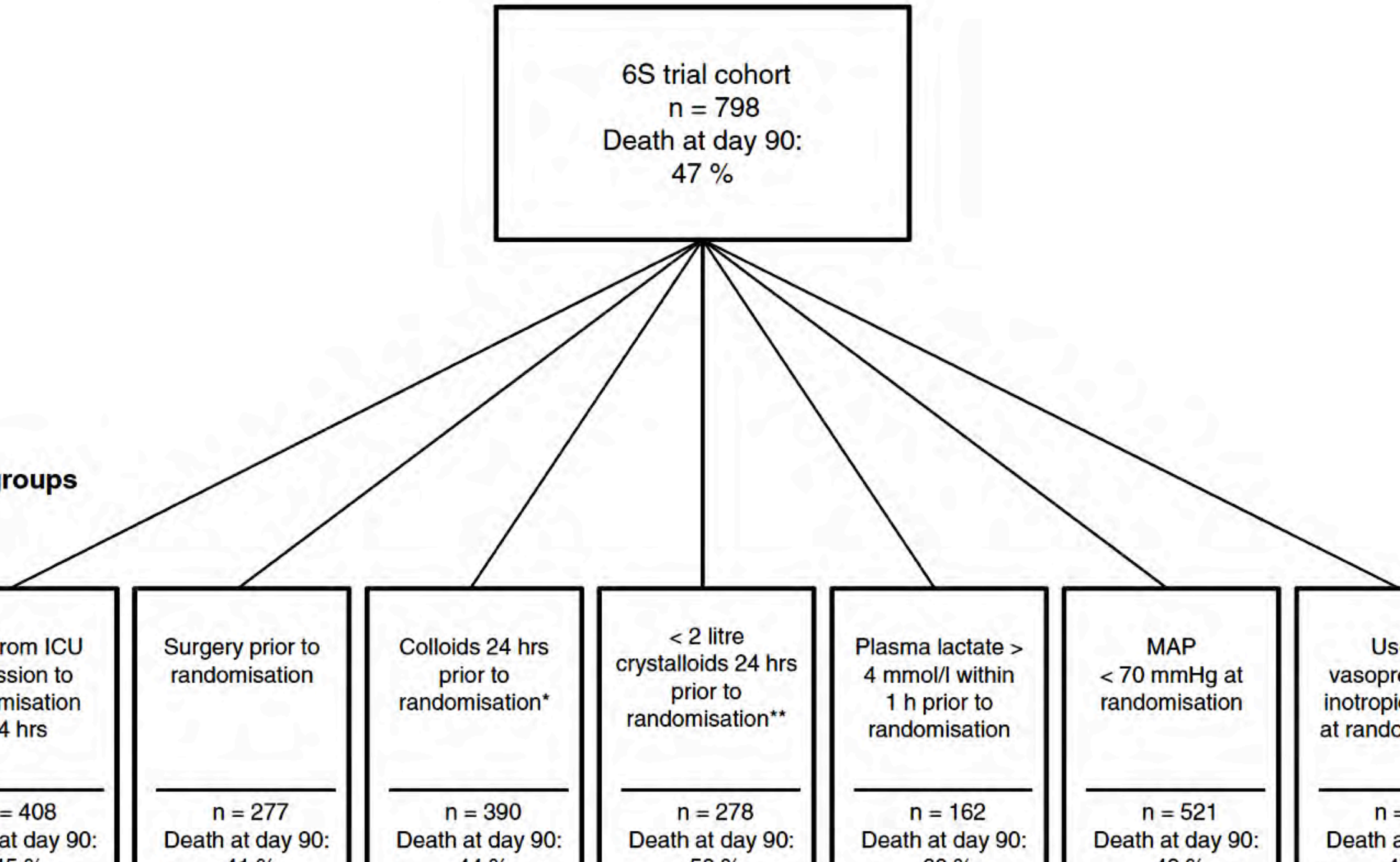


No. at Risk				
HES 130/0.42	398	240	209	197
Ringer's acetate	400	254	240	228

Ringer's Acetate in Severe Sepsis

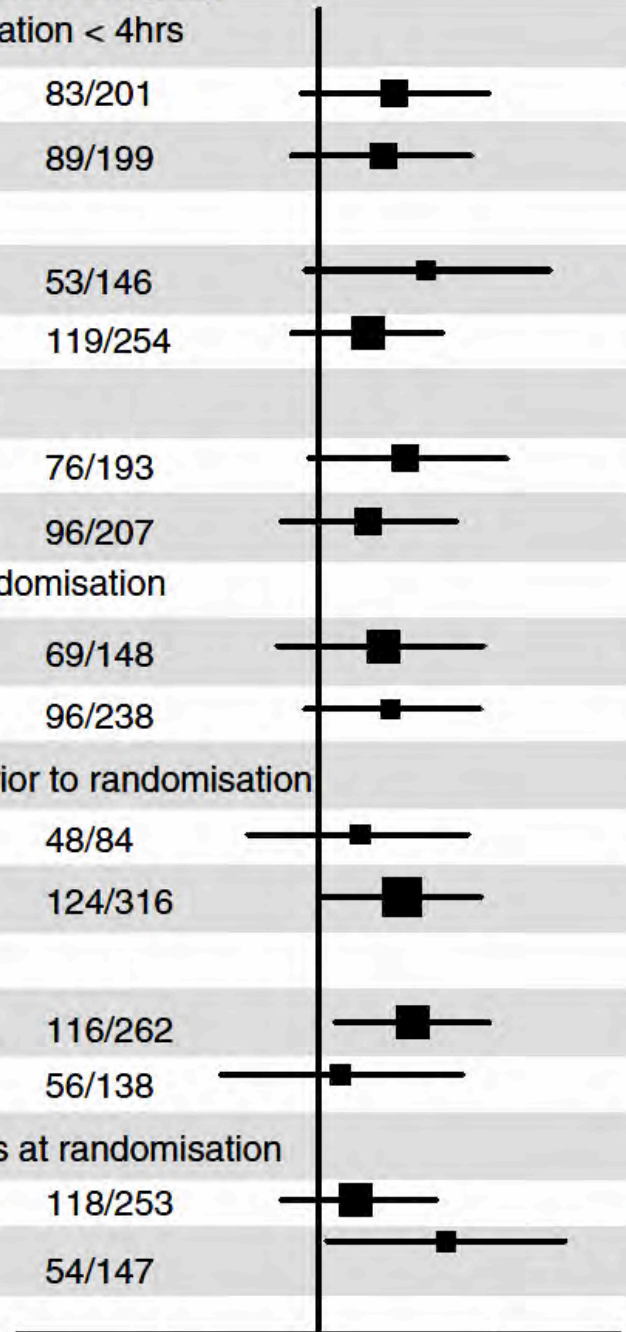


post-hoc analyses of a randomised trial



post-hoc analyses of a randomised trial

Subgroups	HES 130/0.42 no. of events / no. in subgroup	Ringer's acetate	Relative Risk (95% CI)	heterogeneity
Time from ICU admission to randomisation < 4hrs				0.85
Yes	102/207	83/201	1.19 (0.96-1.48)	
No	99/191	89/199	1.16 (0.94-1.42)	
Surgery prior to randomisation				0.42
Yes	61/131	53/146	1.28 (0.97-1.70)	
No	140/267	119/254	1.12 (0.94-1.33)	
Colloids 24 hrs prior to randomisation				0.57
Yes	95/197	76/193	1.22 (0.98-1.54)	
No	101/194	96/207	1.12 (0.92-1.37	
< 2 litre crystalloids 24 hrs prior to randomisation				0.88
Yes	70/130	69/148	1.16 (0.91-1.46)	
No	116/243	96/238	1.18 (0.97-1.45)	
Plasma lactate > 4 mmol/l within 1h prior to randomisation				0.54
Yes	49/78	48/84	1.10 (0.85-1.41)	
No	152/320	124/316	1.21 (1.01-1.45)	
MAP < 70 mmHg at randomisation				0.32
Yes	140/255	116/262	1.24 (1.04-1.48)	
No	61/143	56/138	1.05 (0.80-1.39)	
Use of vasopressor or inotropic agents at randomisation				0.22
Yes	131/256	118/253	1.09 (0.92-1.31)	
No	70/142	54/147	1.34 (1.02-1.76)	



domised trials of 6 % tetrastarch
roxyethyl starch 130/0.4 or 0.42)
severe sepsis reporting mortality:
ematic review and meta-analysis

. Intensive Care Med 2013

Association of Hydroxyethyl Starch
Administration With Mortality and
Kidney Injury in Critically Ill Patients
Requiring Volume Resuscitation
A Systematic Review and Meta-analysis

Zarychanski R. JAMA 2013; 309: 678

resuscitation with 6 % hydroxyethyl
n (130/0.4 and 130/0.42) in acutely ill
nts: systematic review of effects
ortality and treatment with renal
cement therapy

DJ. Intensive Care Med 2013; 39: 558

Hydroxyethyl starch 130/0.38-0.45 versus crystal
or albumin in patients with sepsis: systematic re
with meta-analysis and trial sequential analysis

Haase N. BMJ 2013; 346: 1839

views Nephrology 9, 185 (2013); published online 5 March 2013; doi:10.1038/nrneph.2013.23

L CARE

rious safety concerns regarding use of hydroxyeth
rch for acute fluid resuscitation

URNAL CLUB CRITIQUE

ydroxyethyl starch in severe sepsis: end of arch era?

s A Estrada[1] and Raghavan Murugan[1,2*]

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

October 2013
MA/606303/2013

RAC confirms that hydroxyethyl-starch solutions (HE
hould no longer be used in patients with sepsis or bu
njuries or in critically ill patients

ES will be available in restricted patient populations

patients with severe sepsis: A prospective sequential analysis*

	Hydroxyethyl Starch Period (n = 360)	Gelatin Period (n = 352)	Crystalloid Period (n = 334)
Age, years, median [interquartile range]	69.5 [57.8–76.8]	68.8 [57.7–76.3]	70.2 [58.6–77.6]
Male, n (%)	238 (66.1)	239 (67.9)	226 (67.7)
Comorbidities, n (%)			
Hypertension	169 (46.9)[a]	184 (52.3)[b]	200 (59.9)
Diabetes mellitus	99 (27.5)	109 (31.0)	96 (28.7)
Cancer	74 (20.6)[a]	101 (28.7)	116 (34.7)
Chronic renal failure	18 (5.0)	3 (0.9)	9 (2.7)
Liver cirrhosis	13 (3.6)[c]	27 (7.7)	32 (9.6)
Septic shock, n (%)	295 (81.9)	293 (83.2)	288 (86.2)
Procalcitonin, ng/mL	2.9 [0.8–10.1]	2.3 [0.7–6.7][b]	3.0 [0.8–10.4]
Serum lactate, mmol/L	2.3 [1.3–4.1]	2.1 [1.3–3.8]	1.8 [1.2–3.2]
Central venous oxygen saturation, %	71 [67–74]	70 [66–74]	71 [68–75]
Platelet count, × 10^3/mL	167 [109–241]	141 [49–238][c]	159 [88–258]
Serum creatinine, µmol/L	101 [81–139]	96 [79–130]	96 [81–144]
Creatinine clearance, mL/min	62 [43–89]	66 [48–91]	62 [43–88]
Simplified Acute Physiology Score II score	50 [39–63][b]	52 [40–65]	53 [41–66]
Sequential Organ Failure Assessment score	8 [6–11]	8 [6–10]	8 [6–11]

patients with severe sepsis: A prospective sequential analysis*

Conclusions: Shock reversal was achieved equally fast wi
nthetic colloids or crystalloids. Use of colloids resulted in on
rginally lower required volumes of resuscitation fluid. Bo
v molecular weight hydroxyethyl starch and gelatin may impa
al function. (Crit Care Med 2012; 40:2543–2551)

unit for septic shock

e-and-after study of fluid resuscitation and outcome in patients with septic

ge of fluid treatment from dextran 70 in 2006 to crystalloids and albumin in

	2006 (N = 171)	2008 (N = 161)	p-v
median (25-75 percentiles), years	62 (52-71)	63 (56-72)	0.3
der, F/M, n	57/104	57/114	0.7
weight, median (25-75 percentiles), kg	80 (70-90)	75 (60-90)	0.1
ical admission, n/N (%)	105/171 (61)	86/161 (53)	0.1
II, median (25-75 percentiles)	56 (43-68)[a]	51 (41-62)[b]	0.0
-max in ICU, median (25-75 percentiles)	12 (10-16)[a]	12 (10-16)[b]	0.5
matological malignancy, n/N (%)	29/171 (17%)	22/161 (14%)	0.4
in the ICU, median (25-75 percentiles), days	9 (5-17)	8 (4-13)	0.0
in shock in the ICU[c], median (25-75 percentiles), days	4 (2-7)	4 (2-8)	0.5

unit for septic shock

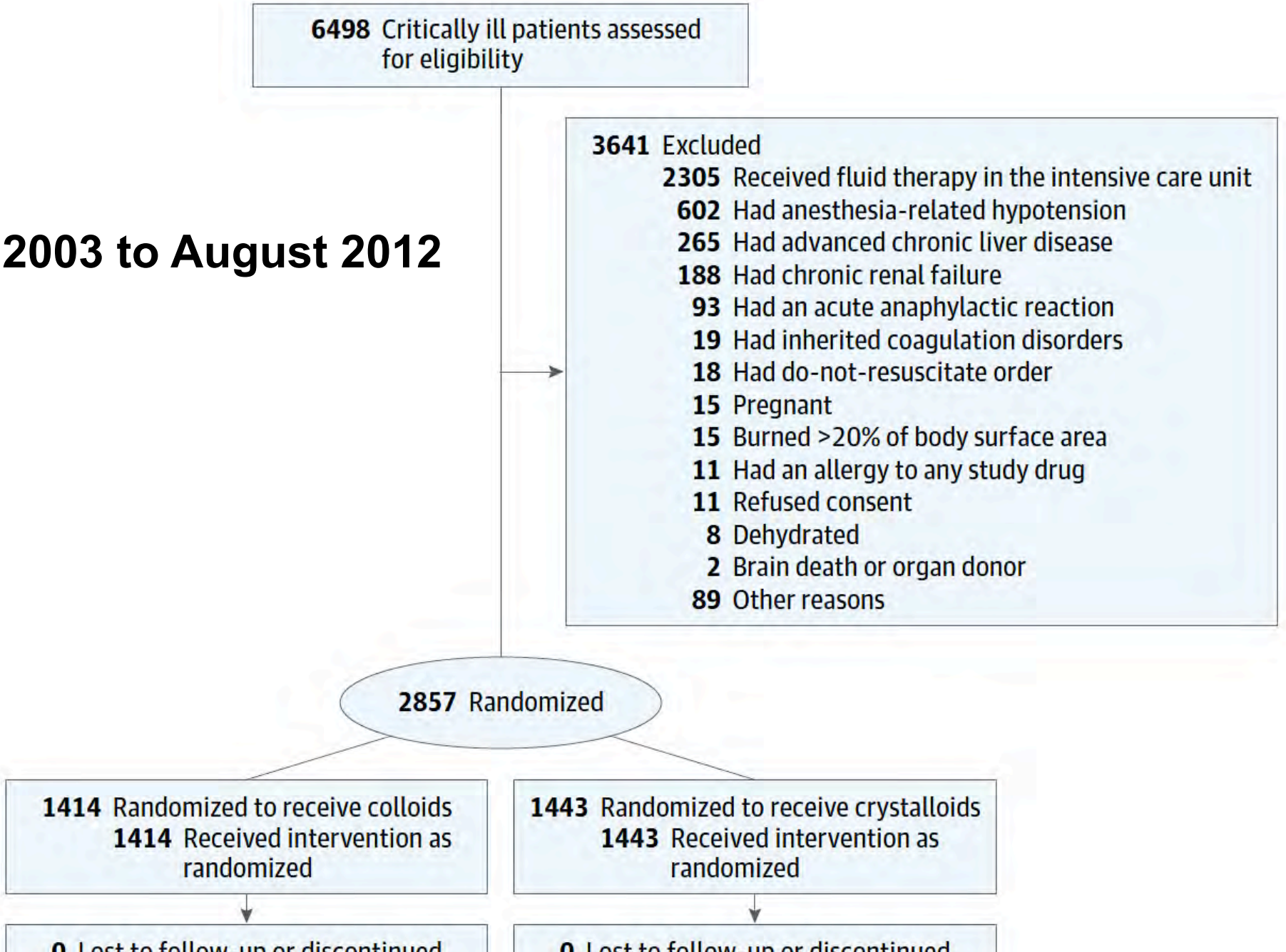
	2006 (N = 171)	2008 (N = 161)	p
replacement therapy[a], n_1/n_2 (%)	71/150 (47)	56/139 (40)	0
nts with ≥ 1 major bleeding event[b], n/N (%)	51/171 (30)	31/161 (19)	0
nortality, n/N (%)	47/171 (27)	47/161 (29)	0
y mortality, n/N (%)	77/171 (45)	83/161 (52)	0

Cumulative doses of Dextran 70 and pts with severe bleeding events

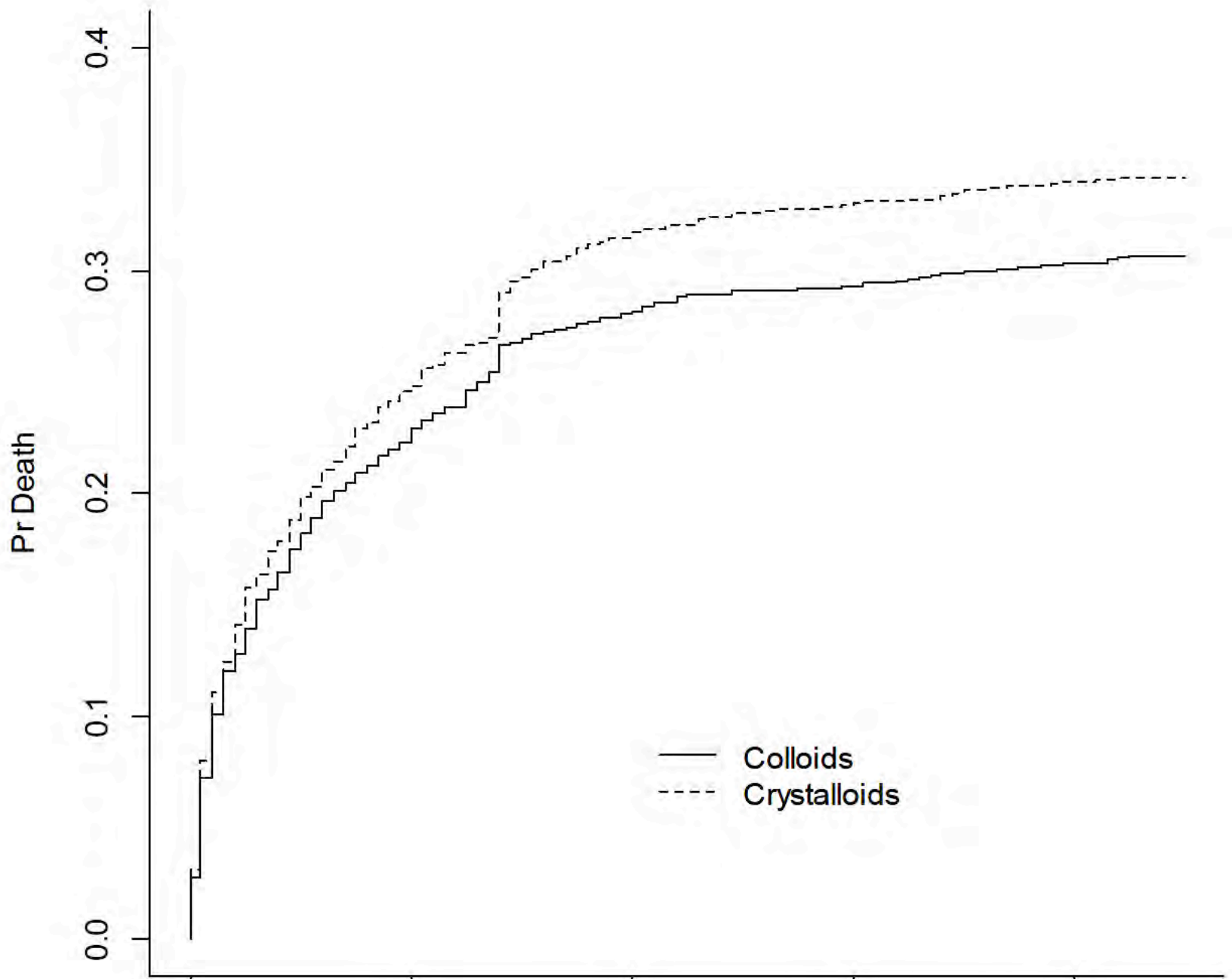
Dosis, ml/kg	2006, n/N (%)	2008, n/N (%)
-25	8/45 (17.8)	15/100 (15.0)
5-50	13/48 (27.1)	4/27 (14.8)
0-75	7/27 (26.0)	3/13 (23.1)
5-100	5/15 (33.3)	4/16 (25.0)

With Hypovolemic Shock
The CRISTAL Randomized Trial

ebruary 2003 to August 2012
s



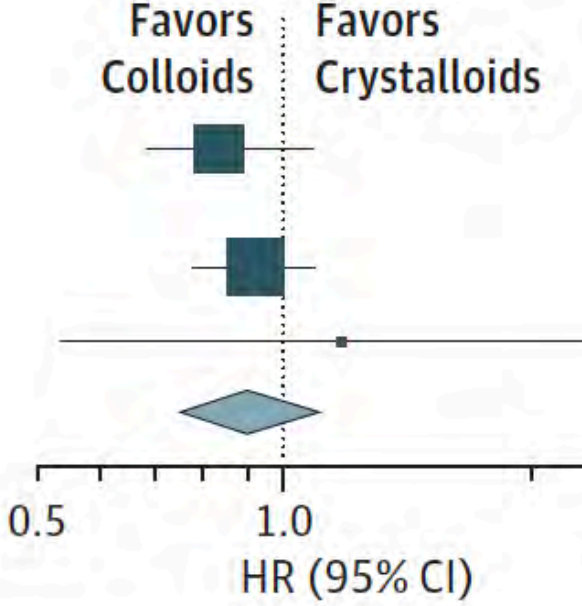
With Hypovolemic Shock
The CRISTAL Randomized Trial



With Hypovolemic Shock
The CRISTAL Randomized Trial

D28 mortality

for ICU on	Colloids Group (n = 1414) No. of Patients	Colloids Group (n = 1414) No. of Deaths	Crystalloids Group (n = 1443) No. of Patients	Crystalloids Group (n = 1443) No. of Deaths	HR (95% CI)
auses of emic shock	555	131	572	152	0.87 (0.69-1.10)
	774	215	779	226	0.95 (0.78-1.10)
	85	13	92	12	1.19 (0.54-2.60)
ents	1414	359	1443	390	0.93 (0.80-1.10)



With Hypovolemic Shock
The CRISTAL Randomized Trial

		Colloids N=1414	Crystalloids N=1443
Isotonic saline			
	— no (%)	252 (17.82)	1236 (85.65)
	volume - ml	1000 [500;2500]	2500 [1500;4500]

dministration prior ICU admission (within the past 12 h)

talloids, No. (%)	526 (37.2)	402 (27.9)
ose, median (IQR), mL	1000 (500-1000)	650 (500-1000)
oids, No. (%)	585 (41.4)	685 (47.5)
ose, median (IQR), mL	1000 (500-2000)	1000 (500-2000)

Gelatins	— no (%)	494 (34.94)	24 (1.66)
	volume - ml	1500 [1000;3000]	1000 [500;2000]
	Duration - days	2 [1;3]	1 [1;1]
Hydroxyethyl starch	— no (%)	973 (68.81)	69 (4.78)
	volume - ml	1500 [1000;2000]	500 [500;1000]
	Duration - days	2 [1;2]	1 [1;1]
Albumin 4%	— no (%)	87 (6.15)	60 (4.16)
	volume - ml	1000 [500;1500]	1000 [500;1500]
	Duration - days	1 [0;3]	1 [0;2]
Albumin 20%	— no (%)	201 (14.21)	177 (12.27)
	volume - ml	300 [200;600]	300 [200;500]

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sepsis and septic shock when patients require substan

amounts of crystalloids (grade 2C).

clusions: Albumin displayed a more favorable safety profile than
lable evidence does not support the existence of consistent safety
s between HES solutions.

with severe sepsis

cteristic	Albumin group ($n = 603$)	Saline group ($n = 615$)	p
nean ± SD in years)	60.5 ± 17.2	61.0 ± 17.1	0.6
r: male (no., %)	359 (59.6)	351 (57.1)	0.3
sion: surgical (no., %)	122 (20.2)	143 (23.3)	0.2
a (no., %)	8 (1.3)	9 (1.5)	1
natic brain injury (no., %)	2 (0.33)	2 (0.33%)	1
respiratory distress syndrome (no., %)	39 (6.5)	42 (6.8)	0.8
HE II[a] score (mean ± SD)	21.6 ± 7.8	21.8 ± 7.7	0.6
arterial pressure (mean ± SD, mmHg)	72.6 ± 15.5	74.5 ± 16.1	0.0
shock[b] (no., %)	209 (34.8)	229 (37.3)	0.3
albumin (mean ± SD ,g/l)	25.0 ± 7.2	25.2 ± 7.4	0.6
replacement therapy (no., %)	23 (3.8)	17 (2.8)	0.3
nical ventilation (no., %)	342 (56.8)	365 (59.4)	0.3

ted Odds ratio for mortality

cteristic		p value	Odds ratio (95
nent assignment	Reference or unit of change		

olutions Improve Mortality in Sepsis?

me	No. of Studies	No. of Participants	Statistical Method	Effect S
lity	17	1,977	OR (95% CI)	0.82 (0.67
lity excluding trials	11	1,683	Risk ratio (95% CI)	0.76 (0.62
Boldt et al				

nfidence interval.

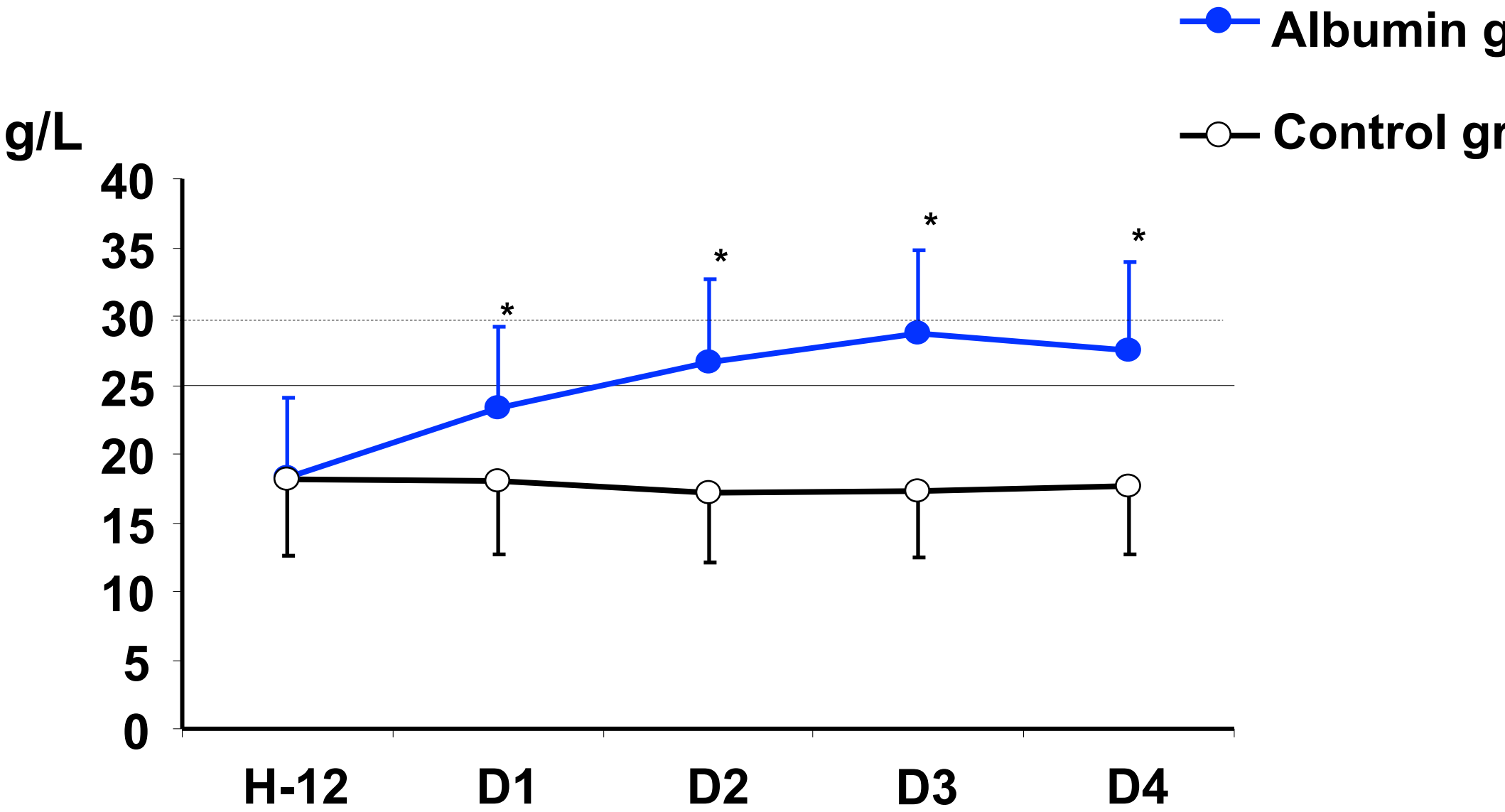
TAKE-HOME MESSAGE

min use during resuscitation of patients with sepsis may decrease mor
mpared with other fluid solutions. Until additional studies are publishe
ans should consider albumin use an option during the initial resuscitati
patients with sepsis

Early Albumin Resuscitation during Septic Shock

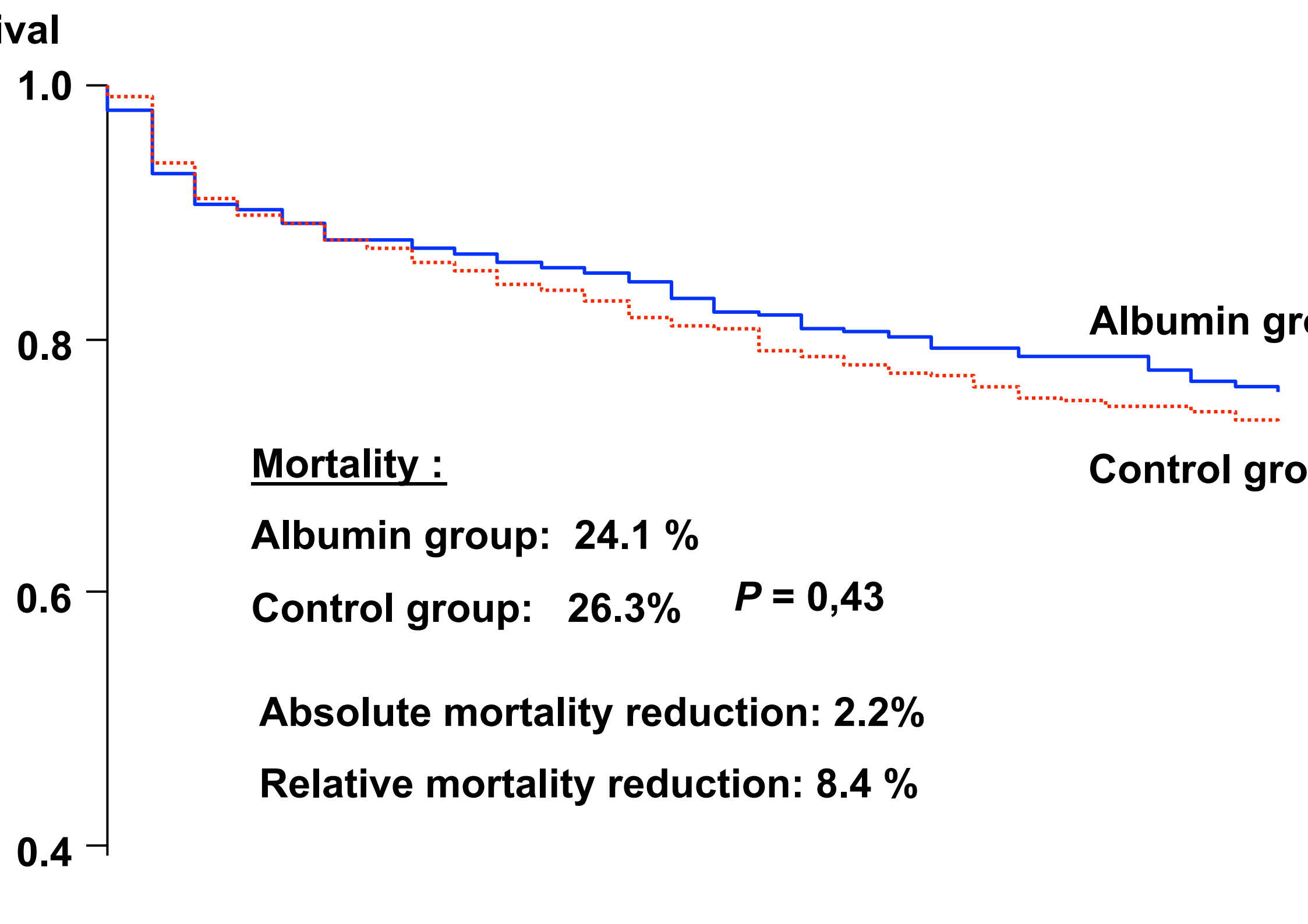
ALBumin Italian Outcome Sepsis study

roduct	20% Albumin
rimary aims	
econdary aims	
atients	
iming administration	
tratification	
dministration	



% of patients with Albuminenia < 25 g/L

	H-12	D1	D2	D3	D4
Albumin group	88	60	38	23	36
Control group	88	91	93	93	93


ival
1.0
0.8
0.6
0.4
Albumin gr
Control gro
Mortality :
Albumin group: 24.1 %
Control group: 26.3%
P = 0,43
Absolute mortality reduction: 2.2%
Relative mortality reduction: 8.4 %

per protocol (n=682)

ath

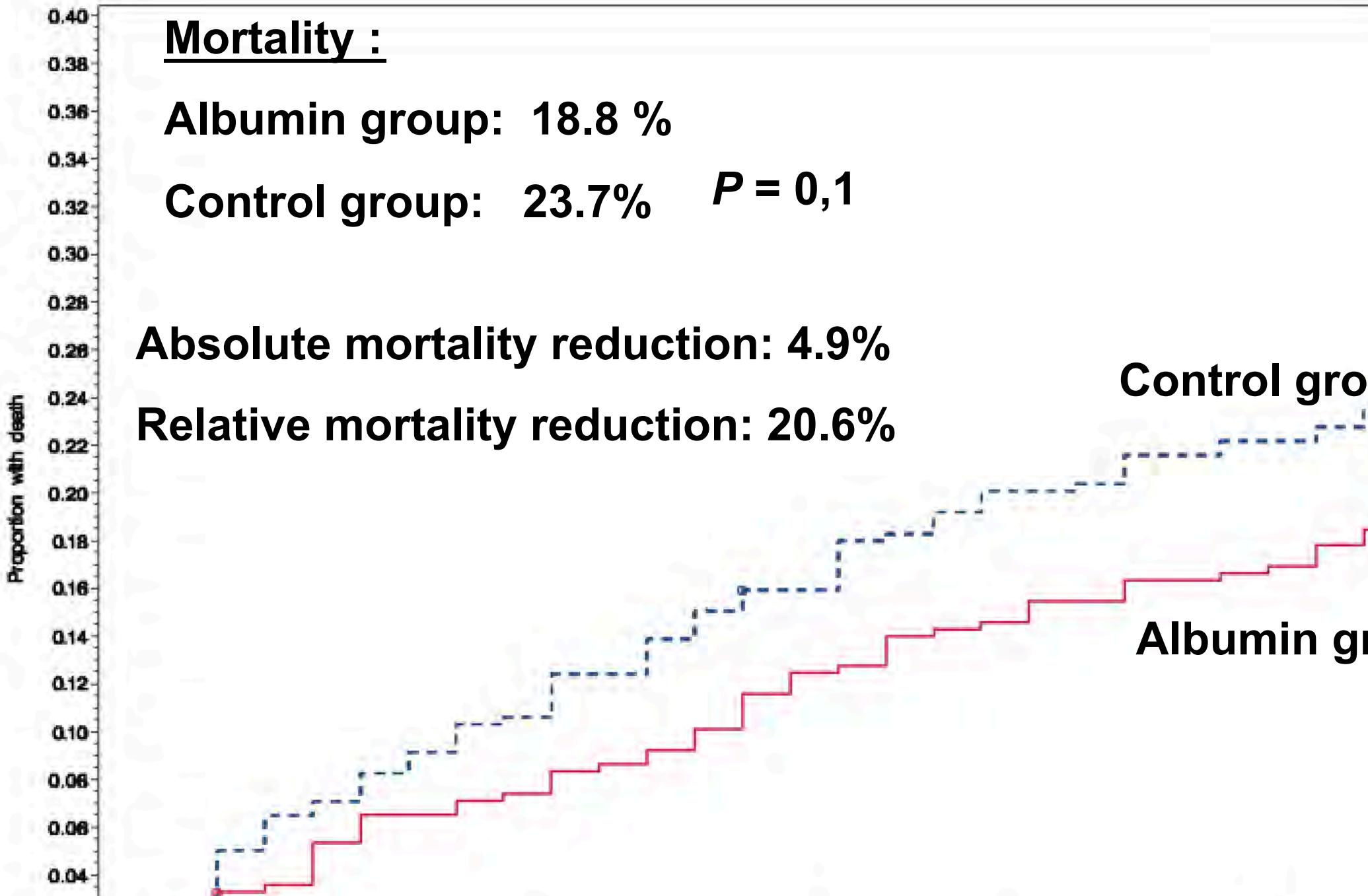
Mortality :

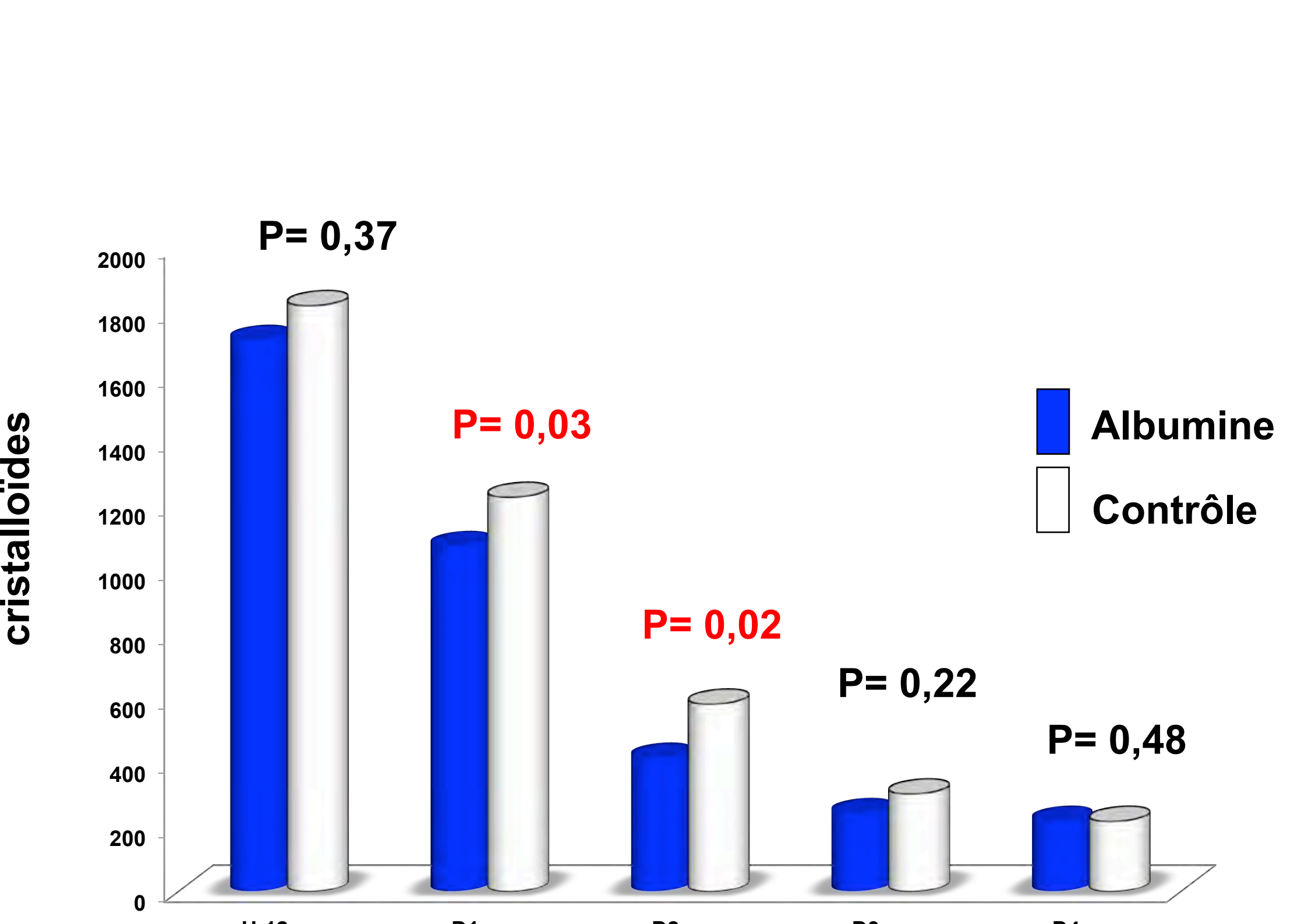
Albumin group: 18.8 %

Control group: 23.7% ***P*** **= 0,1**

Absolute mortality reduction: 4.9%

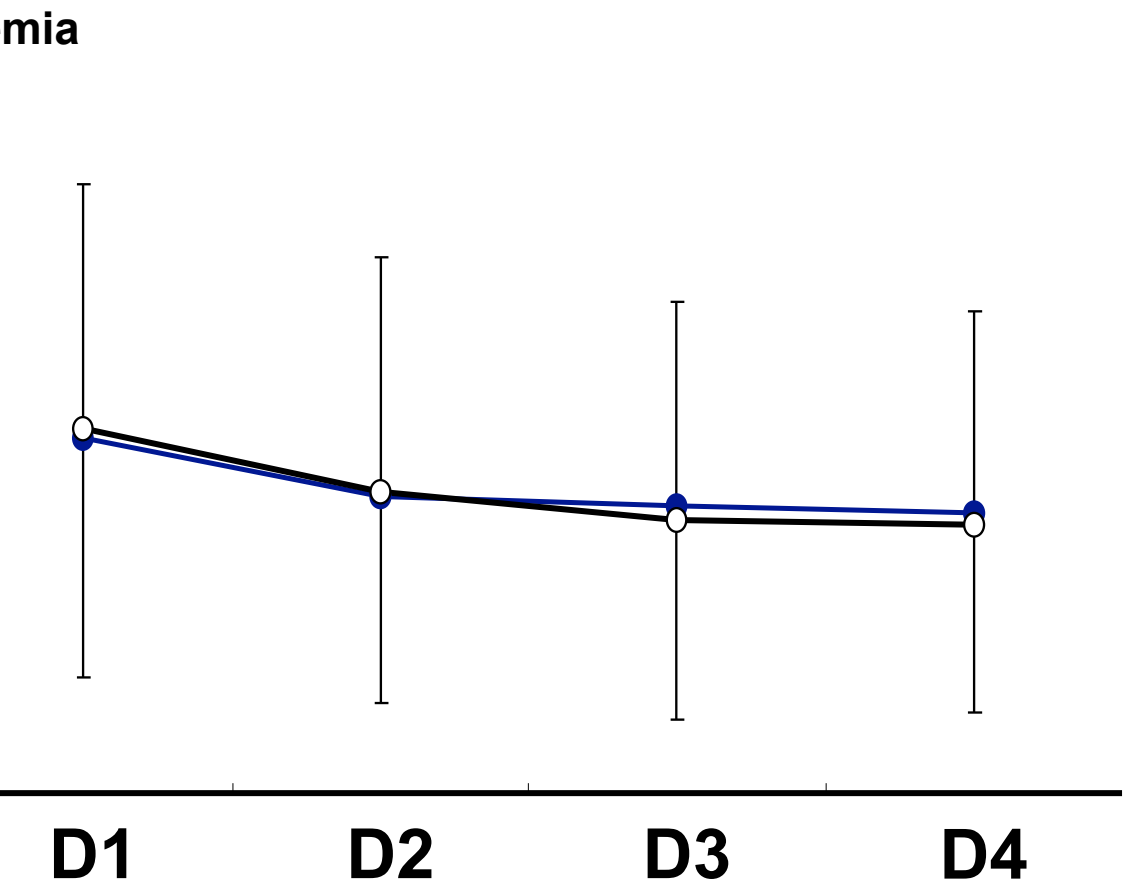
Relative mortality reduction: 20.6%



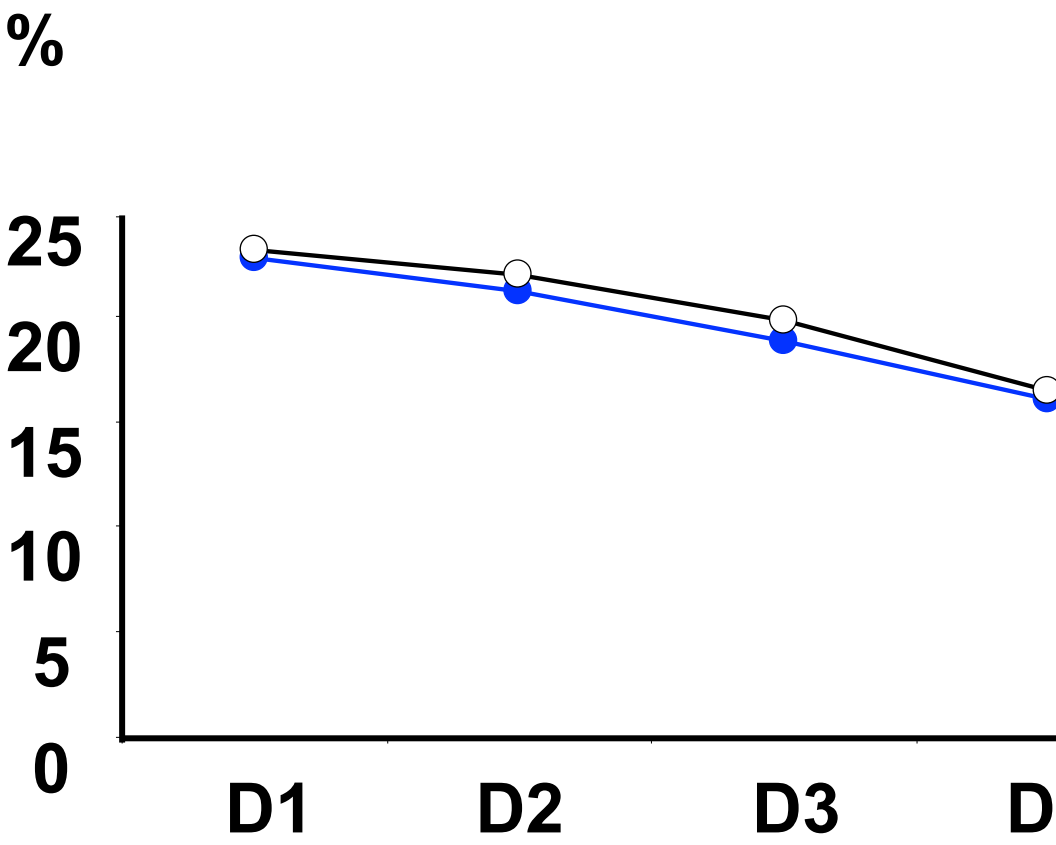

P= 0,37
P= 0,03
P= 0,02
P= 0,22
P= 0,48
2000
1800
1600
1400
1200
1000
800
600
400
200
0
cristalloïdes
Albumine
Contrôle

	Albumin group (n = 399)	Control group (n= 393)	
ortality at D 90	138 (34,7)	138 (35,1)	0,
o of days, median [IQR]			
MV-free within D28	15 [0;23]	13 [0;22]	0,
Catecholamine-free within D28	24 [13,7;26]	23 [8,7;25]	0,03
osocomial infection incidence, No (%)	93 (23,3)	90 (23)	0,
ngth of stay, median [IQR], days			
ICU	11 [5;20]	10,5 [5;21]	0,61
Hospital	24 [13;38]	23 [11;37]	0,

Creatininemia evolution



Patient RRT



	Albumin group	Control group	
RT-free within D28	28 [16;28]	28 [12;28]	0,49

alian Outcome Sepsis study

in patients with severe sepsis or sep

Presentazione | Adesione | Andamento | Materiale | Sottoprogetto Bioumorale | News | Contatti

mmittee:

P. Caironi (Milano), A Pesenti,
(Monza), R. Latini, S. Masson
Tognoni, M. Romero (Santa
CH)

rdinatore:

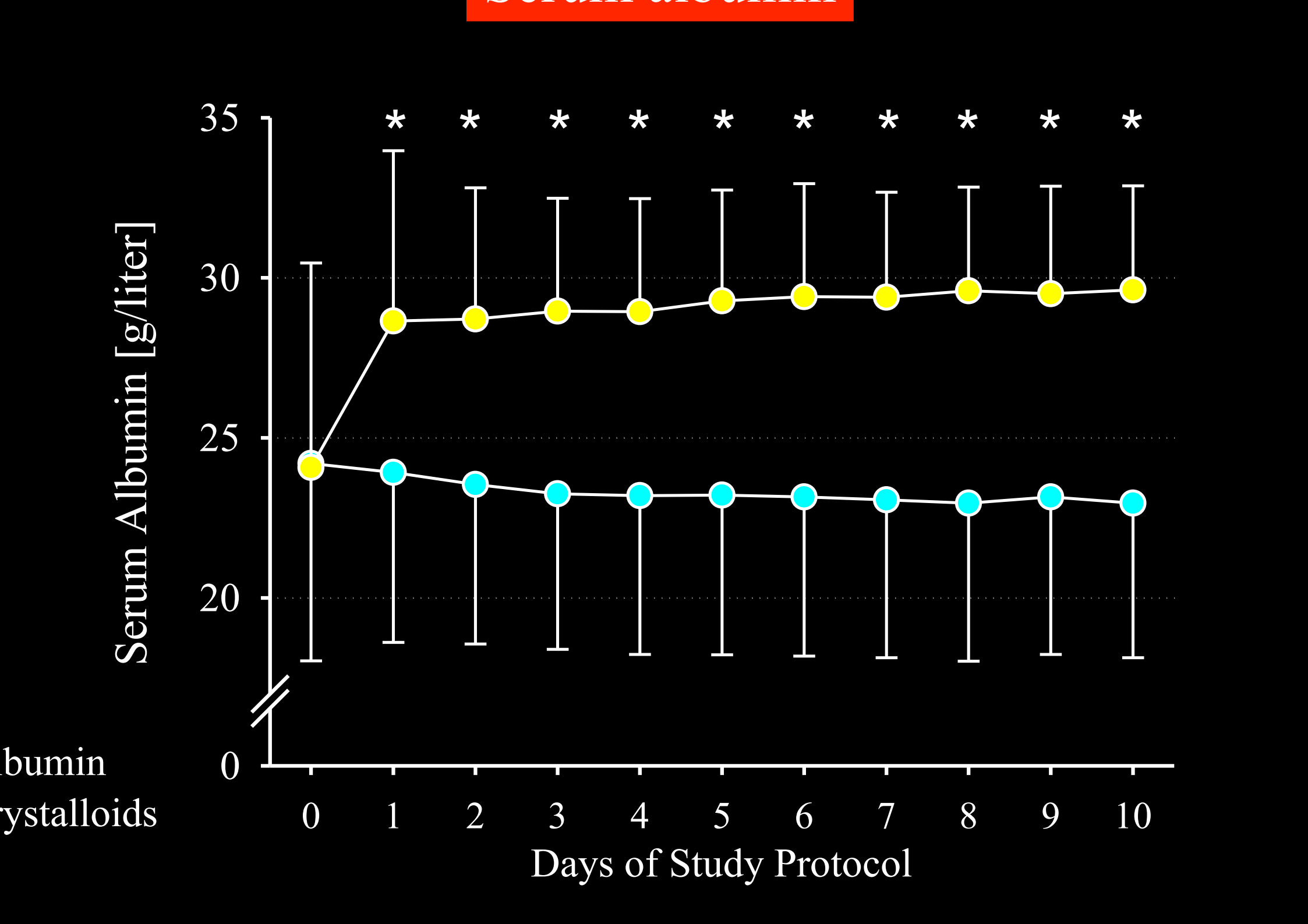
estesiologia e Rianimazione,
IRCCS "Ospedale Maggiore
Mangiagalli, Regina Elena",
egli Studi di Milano.
35 - 20122 Milano.
3232
3230
non@policlinico.mi.it -
i@unimi.it

Tecnico-Scientifica:

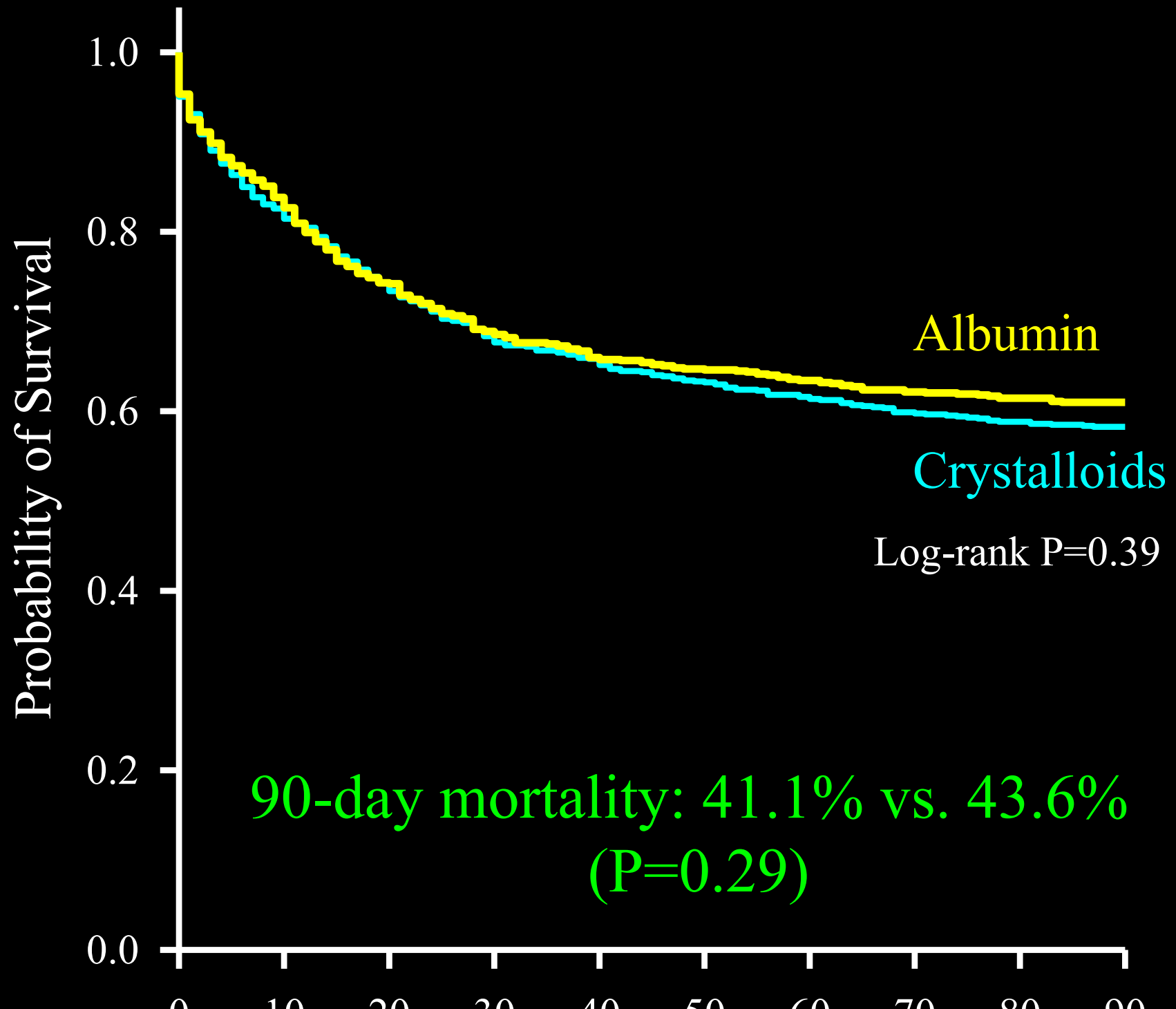
mero, Gianni Tognoni
zzi
ario Negri Sud, Via Nazionale
S. Maria Imbaro (CH)
70 219 - 256 - 258
70 248
s.cssifo@negrisud.it

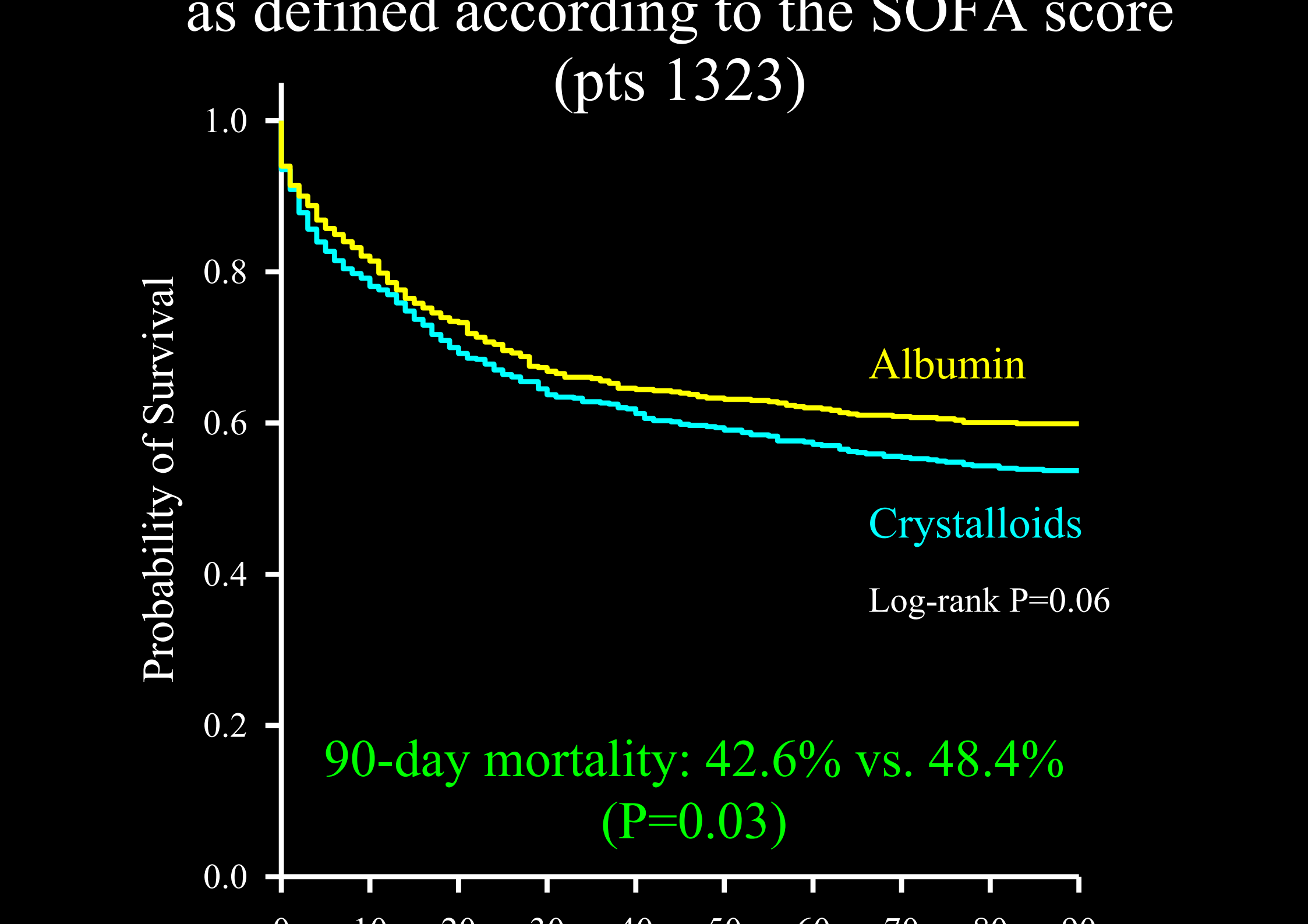
Studio indipendente
su scala nazionale
condotto con
140 centri di Terapia Intensiva
approvato e finanziato
dall'Agenzia Italiana del Farmaco
(AIFA)

	Albumin group (n = 903)	Control group (n= 907)
Age, mean, year	66	66
Male sex,%	60	60
Type of patient, %		
Medical	56.4	57
Unscheduled surgery	7.6	6.4
Elective surgery	35.9	36.4
SAPS2	49.3	49.3
Site of infection		
Abdomen	40	40
Albumin level	24.1	24.2


Serum Albumin
35
30
25
20
0
Serum Albumin [g/liter]
* * * * * * * * * *
0 1 2 3 4 5 6 7 8 9 10
Days of Study Protocol
lbumin
rystalloids

(1810 pts)


Probability of Survival
1.0
0.8
0.6
0.4
0.2
0.0
Albumin
Crystalloids
Log-rank P=0.39
90-day mortality: 41.1% vs. 43.6%
(P=0.29)


as defined according to the SOFA score
(pts 1323)
1.0
0.8
0.6
0.4
0.2
0.0
Probability of Survival
Albumin
Crystalloids
Log-rank P=0.06
90-day mortality: 42.6% vs. 48.4%
(P=0.03)

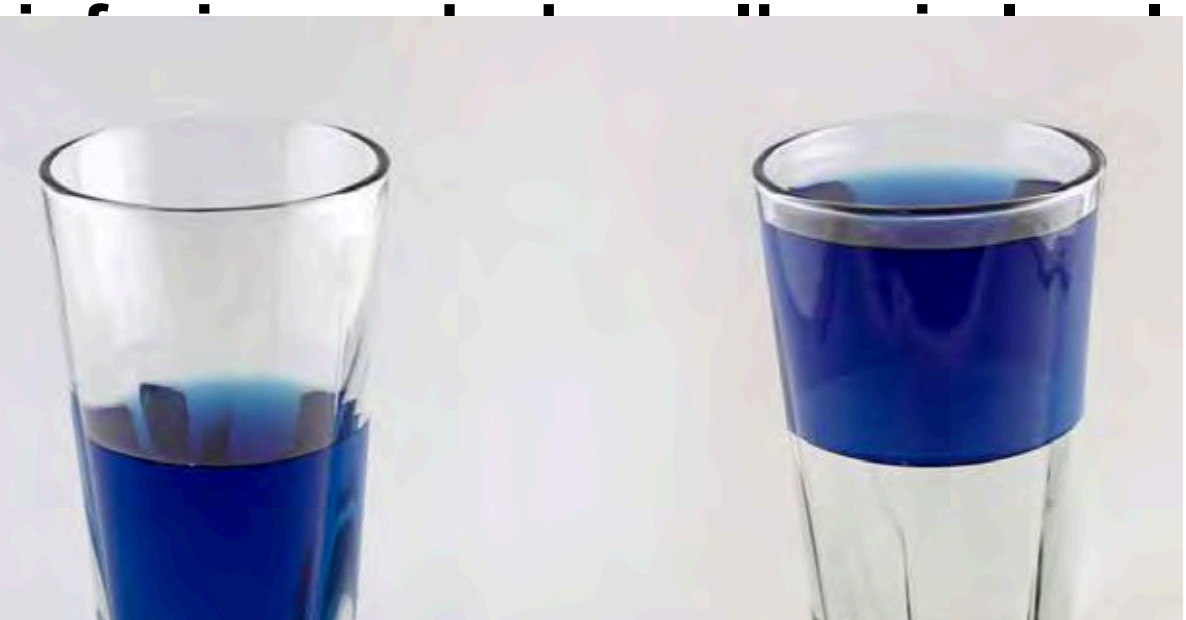
Not at the initial phase → Cristalloids YES but not too much!!

No HES

Avoid gelatin or dextran

Albumin administration might be prescribed after initial crystal

is belo



The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

CRITICAL CARE MEDICINE

Simon R. Finfer, M.D., and Jean-Louis Vincent, M.D., Ph.D., *Editors*

Resuscitation Fluids

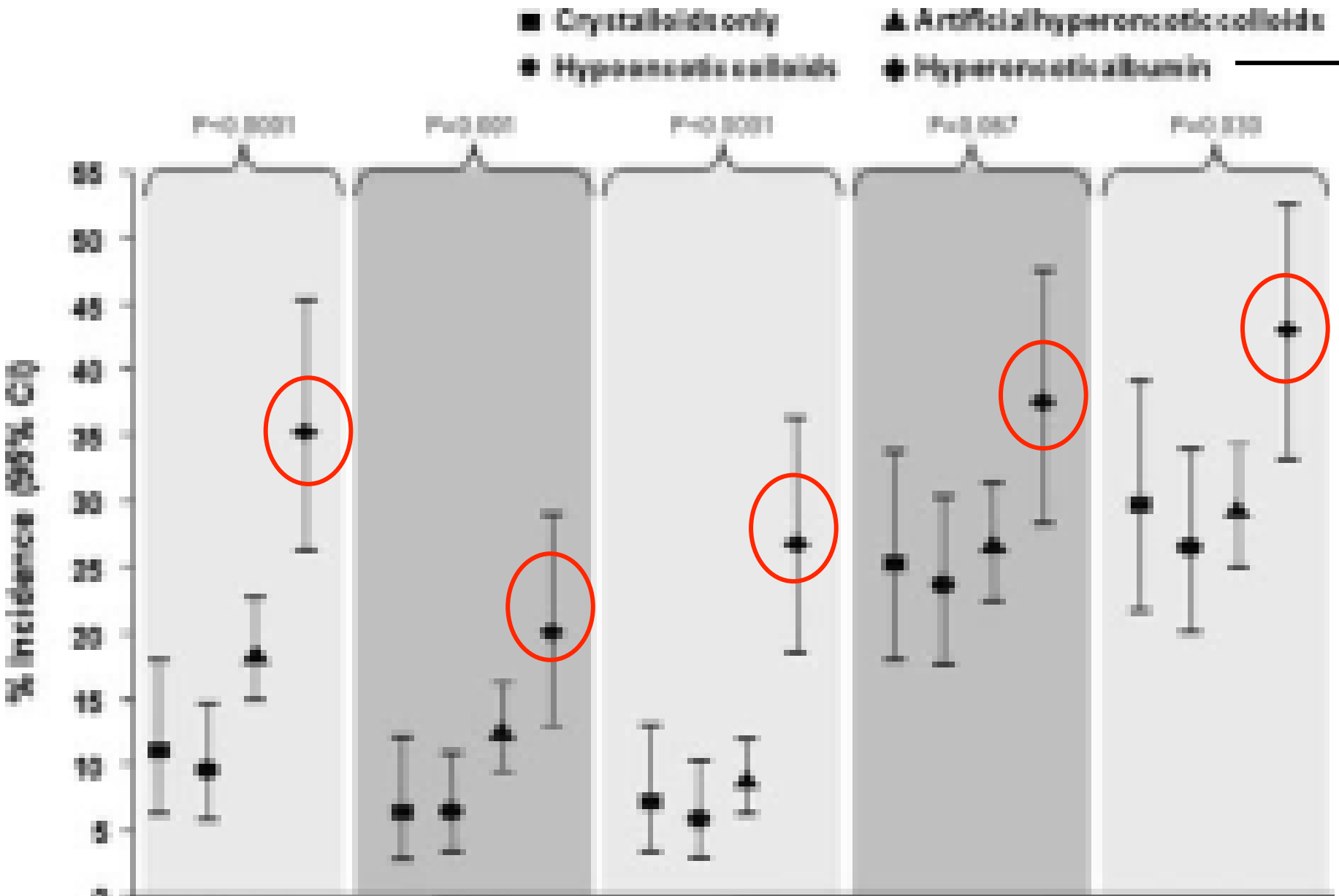
John A. Myburgh, M.B., B.Ch., Ph.D., and Michael G. Mythen, M.D., M.B., B.S.

謝謝您

Laurent Brochard
for the CRYCO Study Group

Cohort study : 822 patients

Risk of renal adverse events in patients with shock



he fluid that is most likely to be lost and replace the fluid lost in equivalent volumes.
serum sodium, osmolarity, and acid–base status when selecting a resuscitation fluid.
cumulative fluid balance and actual body weight when selecting the dose of resuscitation fluid.
the early use of catecholamines as concomitant treatment of shock.

uirements change over time in critically ill patients.

ulative dose of resuscitation and maintenance fluids is associated with interstitial edema.
ical edema is associated with an adverse outcome.
is a normal response to hypovolemia and should not be used solely as a trigger or end point for fluid particularly in the post-resuscitation period.
of a fluid challenge in the post-resuscitation period (≥24 hours) is questionable.
of hypotonic maintenance fluids is questionable once dehydration has been corrected.

considerations apply to different categories of patients.

patients require control of hemorrhage and transfusion with red cells and blood components as indi
balanced salt solutions are a pragmatic initial resuscitation fluid for the majority of acutely ill patient
saline in patients with hypovolemia and alkalosis.
albumin during the early resuscitation of patients with severe sepsis.
isotonic crystalloids are indicated in patients with traumatic brain injury.
is not indicated in patients with traumatic brain injury.
ethyl starch is not indicated in patients with sepsis or those at risk for acute kidney injury.