

The 2024 Guideline on use of Intravenous Albumin from the International Collaboration for Transfusion Medicine Guidelines



[Link to Guidelines](#)

Raza S.
Transfusion Medicine Fellow
Canadian Blood Services | University of Toronto | No relevant COI



Title

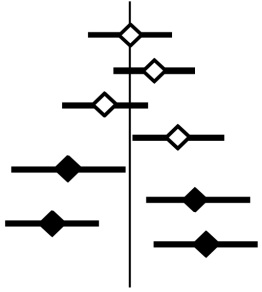
Background

●●● Statements ●●●

Conclusions

Questions

Objectives



To review appraisal of existing evidence used to derive the 2024 ICTMG intravenous albumin guidelines.

Grade of recommendation	Strong recommendation	Weak recommendation	Strong recommendation	Weak recommendation
Conclusions of evidence	Highly certain & benefits	Benefits vs risk & burdens	Benefits vs risks & burdens	No benefit / Potentially harm
Conclusions of evidence	Strong recommendation based on high level of evidence	Moderate recommendation based on high level of evidence	Weak recommendation based on high level of evidence	Recommendation based on high level of evidence
Conclusions of evidence	Strong recommendation based on moderate/low level of evidence	Moderate recommendation based on moderate/low level of evidence	Weak recommendation based on moderate/low level of evidence	Recommendation based on moderate/low level of evidence
Conclusions of evidence	Strong recommendation based on expert opinion	Moderate recommendation based on expert opinion	Weak recommendation based on expert opinion	Recommendation based on expert opinion

To review ICTMG recommendations for the use of intravenous albumin.



To setup discussion with the *Breakthroughs in blood* expert panel following the presentation

Background



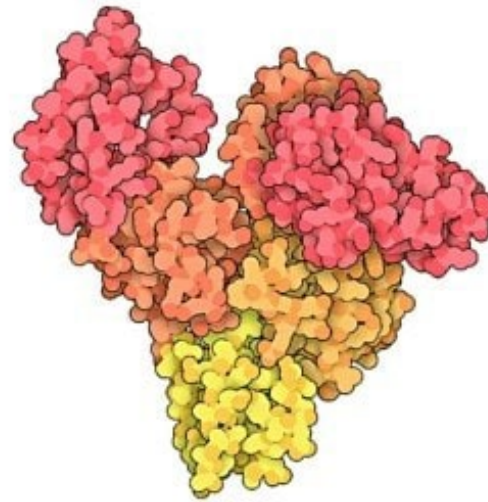
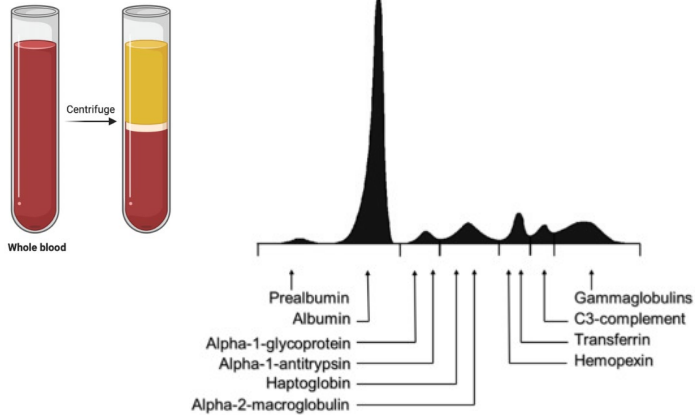
Sarah, 51-year old ♀, alcohol-related liver disease
Admitted hepato-pulmonary syndrome

The admitting physician is struggling because the patient is both hypotensive (low pressure) and anasarctous (diffusely swollen)

She wants to switch the patient from 0.9% saline infusion to a **5% albumin** for hypotension and peritonitis

Albumin

The most abundant plasma protein

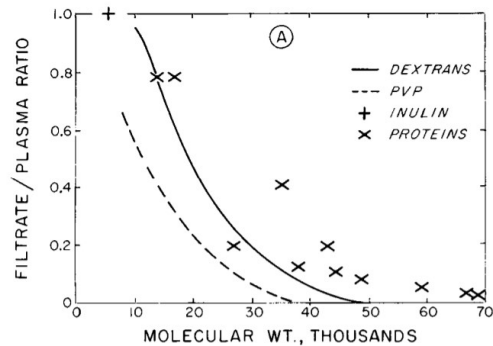


Albumin binds

- Water
- Electrolytes (Na/K/Ca)
- Hormones
- Fatty acids, fatty vitamins
- Bilirubin
- Thyroxine
- Drugs

Albumin is a 67 kilo dalton protein

Negligible clearance due to (-) and wt

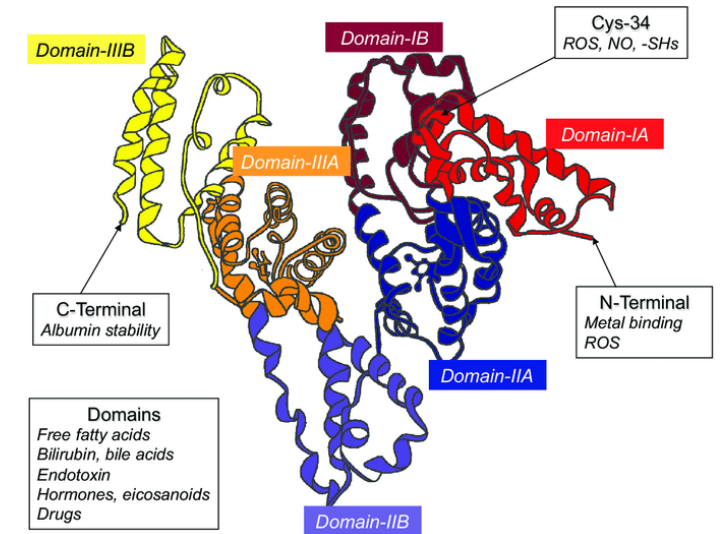


NEJM. 1974 Apr 4;290(14):785-92

Albumin buffers pH

Some antioxidant effect

Albumin confers oncotic pressure



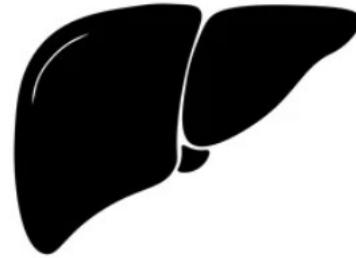
Physiology

Kwashiorkor (malnourishment)
Celiac disease (malabsorption)

Synthetic liver dysfunction

Increased transfer
Redistribution

Food (Amino Acids)



Synthesized in liver at 16 g / day
e.g. 70 kg person, 5L blood
Makes ~ 3 g/L daily



[Link to Guidelines](#)

60% extravascular



40% intravascular

endothelium

Typical plasma albumin concentration
35 to 50 g/L (3.5 to 5.0 g/dL)
(about 200 g in a 5L blood volume)

Under healthy conditions

Exchange rate is 5% per hour

10% metabolized per day

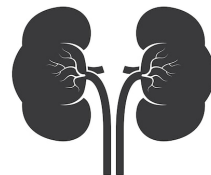
30 mg Renal filtration

1% Gastrointestinal loss

Hypermetabolism



Nephrotic
Syndrome



Protein-Losing
Enteropathy



Oncotic Pressure

extravascular \longleftrightarrow endothelium \longleftrightarrow intravascular



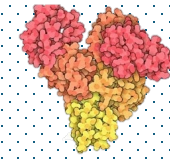
Albumin confers 80% of blood oncotic pressure (partly direct, partly via ion binding)

Oncotic Pressure in *Deranged* Physiology

extravascular \longleftrightarrow endothelium \longleftrightarrow intravascular

Interstitium

Oncotic Pressure



Blood Vessel

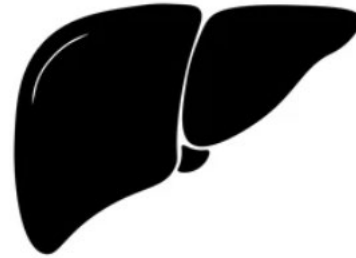
Oncotic Pressure

Net Result:

Low intravascular blood pressure (hypotension)
High extravascular fluid (swelling)

Deranged Physiology

Food (Amino Acids)



Negative Acute Phase Reactant

↑↑ extravascular ↔ endothelium ↓↓ intravascular

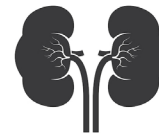
Under critical illness

Exchange rate ↑↑

↑↑↑ metabolized per day



--/↑↑ Renal filtration



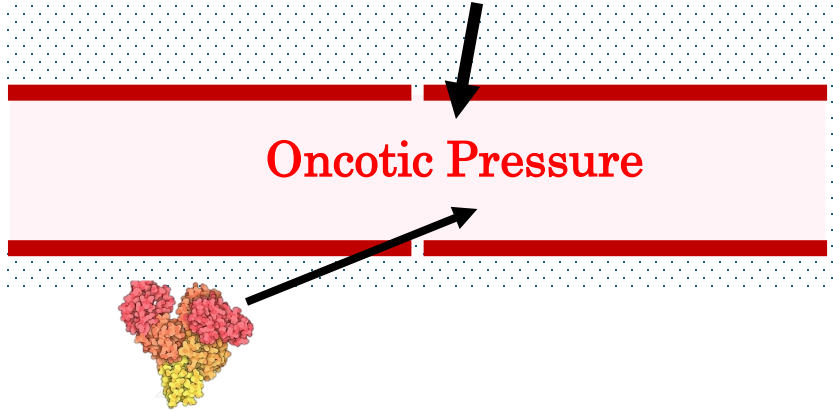
↑↑↑ Gastrointestinal loss



↑↑ Skin

Albumin Transfusion

Interstitial



Rationale

Albumin formulations

5% (or 5 g / 100 ml, or 50 g / L**)

20-25% (or 25 g / 100 ml) -- Hyperosmotic

5% given up to 5 ml/min

25% given up to 2 ml/min

Vial sizes

50 ml, 100 ml, 250 ml, 500 ml

Risks

Transfusion Associated Circulatory Overload, Hypotension, Anaphylaxis, More RBC Transfusions, Peripheral gangrene

Costs

5% is \$40 USD per 100 ml

25% is \$60 USD per 100 ml

48h infusion of 5% alb at 1 ml/kg/hr is about \$3,000
NS would be \$50-100

The 5 billion + “plasma economy” is rife with scandals worldwide

Donors are often marginalized
Donors can be injured by adverse reactions
Donors often misreport on donor questionnaires

Ethics

Title

Background

●●● Statements ●●●

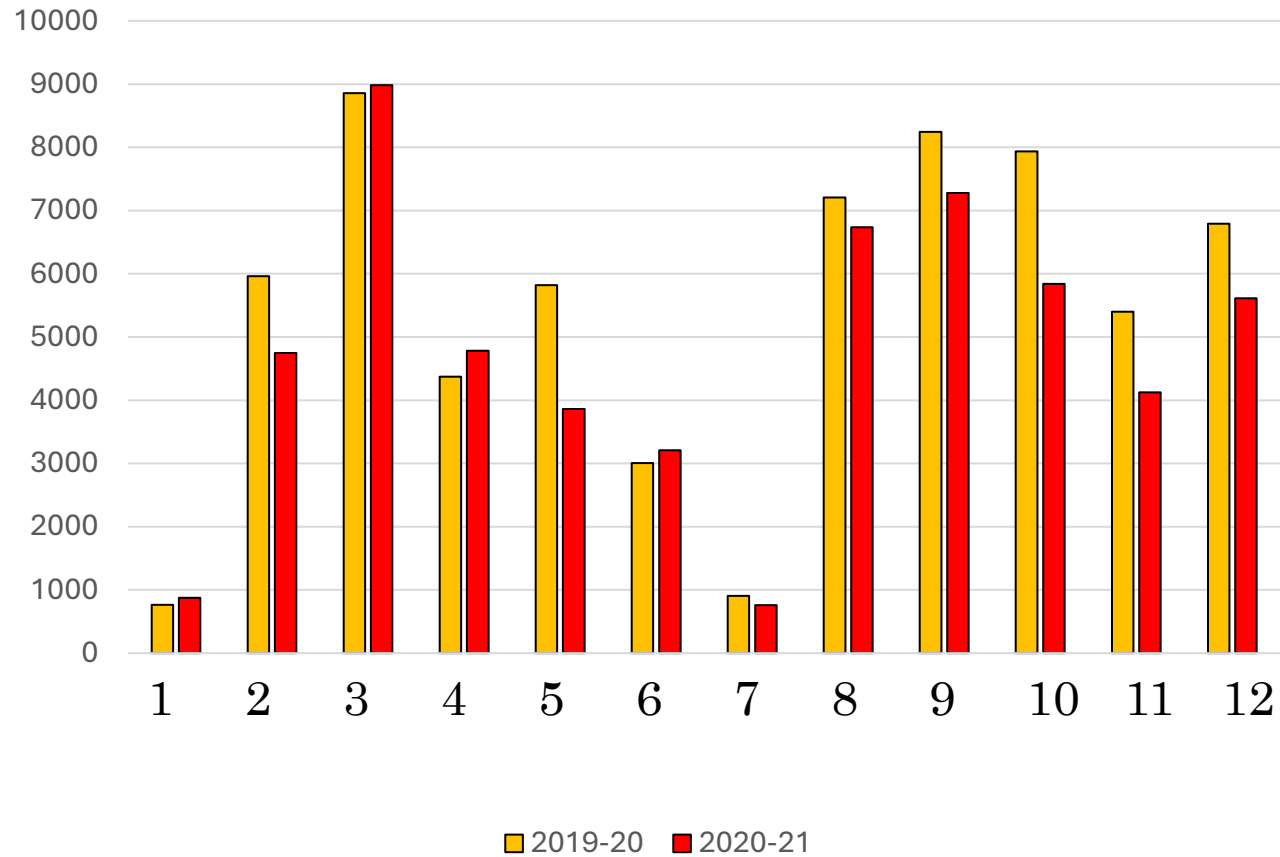
Conclusions

Questions

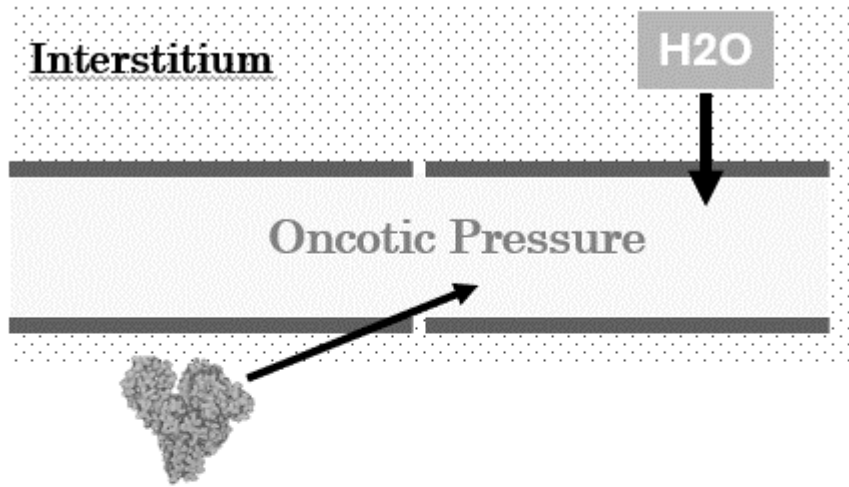


Prevailing Albumin Practice

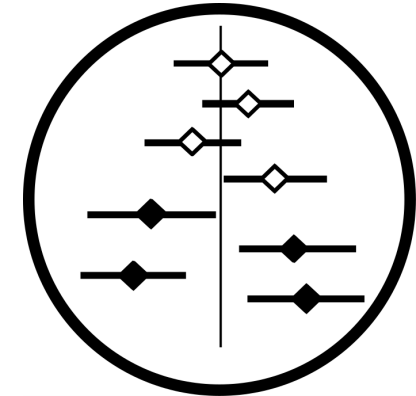
Highly variable



Methodology Preamble

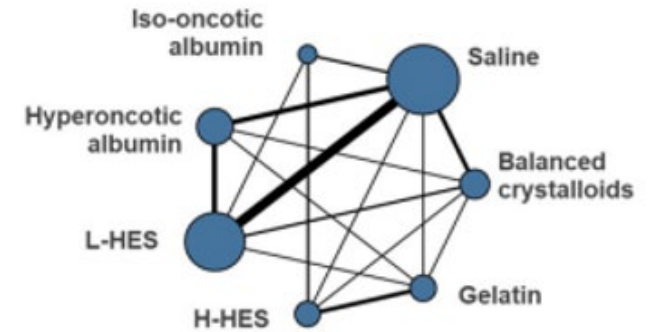


?



Risk of Bias

	A	B	C	D	E	F
	-	?	-	-	?	-
	+	+	+	-	?	-
	+	+	+	-	?	-

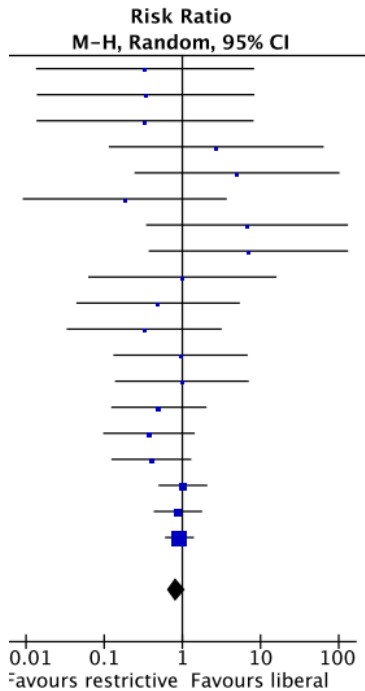
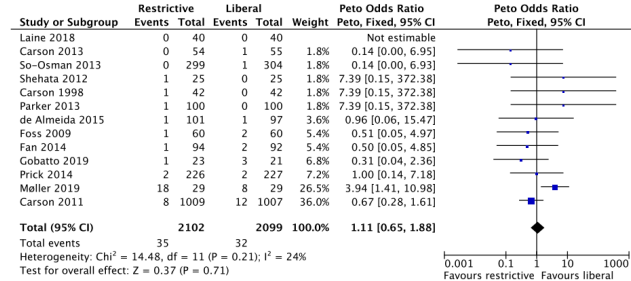


Methodology Preamble

Methods

1. Systematic Review

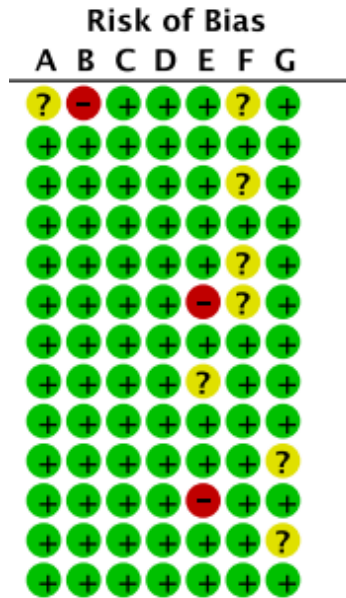
efigure 7: Thromboembolism



2. Risk of Bias Assessment

Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias): Objective measures
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias



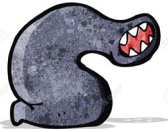
3. GRADE Methodology





Grade of recommendation	I Strong recommendation to do	Ila Moderate recommendation to do	Iib Weak recommendation to do	III Recommendation not to do
Conclusions of evidence	Benefits >>> risk & burdens	Benefits >> risk & burdens	Benefits >= risks & burdens	No benefit / Potentially harm
A High level of evidence	Consistent evidence from well performed and high quality studies or systematic reviews (low risk of bias, direct, consistent, precise)	Moderate recommendation based on high level of evidence	Weak recommendation based on high level of evidence	Recommendation based on high level of evidence
B Moderate / Low level of evidence	Evidence from studies or systematic reviews with few important limitations	Moderate recommendation based on moderate/ low level of evidence	Weak recommendation based on moderate/ low level of evidence	Recommendation based on moderate/ low level of evidence
C Very low level of evidence	Evidence from studies with serious flaws. Only expert opinion, or standards of care	Moderate recommendation based on very low level of evidence	Weak recommendation based on very low level of evidence	Recommendation based on very low level of evidence

Wording in recommendations:

We recommend	We suggest	We might suggest	We do not recommend
We should	Is reasonable	Might be	Should not be performed
Is recommended	Is probably recommended	reasonable	Is not useful
Is indicated	Can be useful	considered	Is not beneficial
Is useful	Can be beneficial	Usefulness is unknown	Is not effective
Is beneficial	Can be effective		Is potentially harmful
Is effective			

Methodology Preamble



Grade of recommendation	I Strong recommendation to do	Ila Moderate recommendation to do	Ilb Weak recommendation to do	III Recommendation not to do
Conclusions of evidence	Benefits >>> risk & burdens	Benefits >> risk & burdens	Benefits >= risks & burdens	No benefit / Potentially harm
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C Very low level of evidence Evidence from studies with serious flaws. Only expert opinion, or standards of care		Moderate recommendation based on very low level of evidence Diverging expert opinions	Weak recommendation based on very low level of evidence Diverging expert opinions	
Wording in recommendations:				
	We recommend We should	We suggest Is reasonable	We might suggest Might be	We do not recommend

Strength of evidence ↑

Benefit ← → Harm

Guideline

Use of Intravenous Albumin

A Guideline From the International Collaboration for Transfusion Medicine Guidelines

*Jeannie Callum, MD; Nikolaos J. Skubas, MD; Aarti Bathla, MPharm, MPH; Homa Keshavarz, PhD; Edward G. Clark, MD; Bram Rochweg, MD; Dean Fergusson, PhD; Sesmu Arbous, MD; Seth R. Bauer, PharmD; Louise China, MD; Mark Fung, MD; Rachel Jug, MD; Michael Neill; Cary Paine, MD; Katerina Pavenski, MD; Prakesh S. Shah, MD; Susan Robinson, MD; Hua Shan, MD; Zbigniew M. Szczepiorkowski, MD, PhD; Thierry Thevenot, MD; Bovey Wu, MD; Simon Stanworth, MD, PhD; and Nadine Shehata, MD; on behalf of the International Collaboration for Transfusion Medicine Guidelines Intravenous Albumin Guideline Group**



Collaborative of volunteers (full and project members) with a focus on rigorous guideline development methodology and implementation, engaging representatives from relevant disciplines, societies, and patient groups.

JAMA | Special Communication

Red Blood Cell Transfusion 2023 AABB International Guidelines

Jeffrey L. Carson, MD; Simon J. Stanworth, MD, DPhil; Gordon Guyatt, MD; Stacey Valentine, MD, MPH; Jane Dennis, PhD; Sara Bakhtary, MD; Claudia S. Cohn, MD, PhD; Allan Dubon, MLS; Brenda J. Grossman, MD, MPH; Gaurav K. Gupta, MD, PhD; Aaron S. Hess, MD, PhD; Jessica L. Jacobson, MD; Lewis J. Kaplan, MD; Yulia Lin, MD; Ryan A. Metcalf, MD; Colin H. Murphy, MD; Katerina Pavenski, MD; Micah T. Prochaska, MD; Jay S. Raval, MD; Eric Salazar, MD, PhD; Nabih H. Saifee, MD, PhD; Aaron A. R. Tobian, MD, PhD; Cynthia So-Osman, MD, PhD; Jonathan Waters, MD; Erica M. Wood, MD; Nicole D. Zantek, MD, PhD; Monica B. Pagano, MD

REVIEW

Red blood cell specifications for patients with hemoglobinopathies: a systematic review and guideline

Veerle Compernelle,¹ Stella T. Chou,² Susano Tanael,³ William Savage,⁴ Jo Howard,⁵ Cassandra D. Josephson,⁶ Isaac Odame,⁷ Christopher Hogan,⁸ Gregory Denomme,⁹ and Nadine Shehata,^{3,10} for the International Collaboration for Transfusion Medicine Guidelines

JAMA | Special Communication

Patient Blood Management Recommendations From the 2018 Frankfurt Consensus Conference

Markus M. Mueller, MD; Hans Van Remoortel, PhD; Patrick Meybohm, MD, PhD; Kari Aranko, MD, PhD; Cécile Aubron, MD, PhD; Reinhard Burger, PhD; Jeffrey L. Carson, MD, PhD; Klaus Cichutek, PhD; Emmy De Buck, PhD; Dana Devine, PhD; Dean Fergusson, PhD; Gilles Folléa, MD, PhD; Craig French, MB, BS; Kathrine P. Frey, MD; Richard Gammon, MD; Jerrold H. Levy, MD; Michael F. Murphy, MD, MBBS; Yves Ozier, MD; Katerina Pavenski, MD; Cynthia So-Osman, MD, PhD; Pierre Tiberghien, MD, PhD; Jimmy Volmink, DPhil; Jonathan H. Waters, MD; Erica M. Wood, MB, BS; Erhard Seifried, MD, PhD; for the ICC PBM Frankfurt 2018 Group



ELSEVIER

Contents lists available at ScienceDirect

Transfusion Medicine Reviews

journal homepage: www.tmreviews.com



Original Articles

Guidance on Platelet Transfusion for Patients With Hypoproliferative Thrombocytopenia



See Editorial, pages 1–2

Susan Nahirniak^{a,*}, Sherrill J. Slichter^b, Susano Tanael^c, Paolo Rebulla^d, Katerina Pavenski^e, Ralph Vassallo^f, Mark Fung^g, Rene Duquesnoy^h, Chee-Loong Sawⁱ, Simon Stanworth^j, Alan Tinmouth^k, Heather Hume^l, Arjuna Ponnampalam^m, Catherine Moltzanⁿ, Brian Berry^o, Nadine Shehata^p, for the International Collaboration for Transfusion Medicine Guidelines (ICTMG)

The ICTMG secretariat is hosted by Canadian Blood Services, the primary funder for ICTMG

Albumin Guideline Development Group

The international panel of expert volunteers for this guideline included:

CANADA

Jeannie Callum*
Aarti Bathla
Homa Keshavarz
Edward G. Clark
Bram Rochweg
Michael Neil**
Dean Fergusson*
Katerina Pavenski*
Prakesh S. Shah
Bovey Wu
Nadine Shehata*

USA

Nikolaos J. Skubas
Seth R. Bauer
Mark Fung*
Rachel Jug*
Cary Paine
Hua Shan
Zbigniew M. Szczepiorkowski*

NETHERLANDS

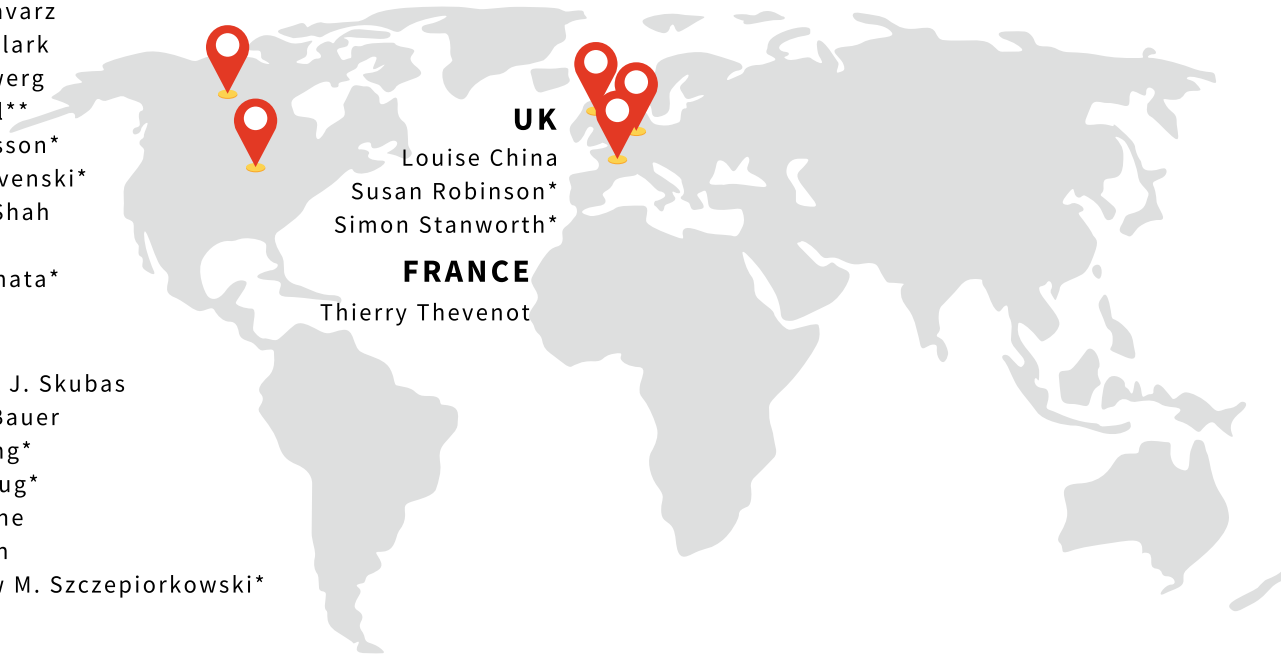
Sesmu Arbous

UK

Louise China
Susan Robinson*
Simon Stanworth*

FRANCE

Thierry Thevenot



* denotes ICTMG full membership at the time of guideline development

** indicates patient representation

Visit www.ICTMG.org

Scope

Appropriate use of albumin in

Liver disease

Critical Care

Renal
replacement

Pediatric and
Neonatal

CV Surgery

Not assessed: Plasma Exchange

Intended primarily to inform

Nephrologists

Anesthesiologists

Lab Technologists

Hematologists

CV Surgeons

Pharmacists

Intensivist

Pathologists

Researchers

Hospitalists

TM Physicians

Patients/Families

General Internists

Hepatologists

Gastroenterologists



[Link to Guidelines](#)

Methods

Co-chairs (2)

Guideline Panel

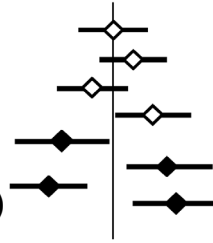
Methodologists

Clinicians

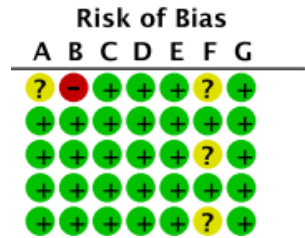
Researchers

Patient Representative

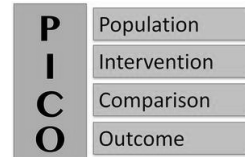
Systematic Review and Meta-Analyses were screened or conducted (**PROSPERO + PRISMA**)



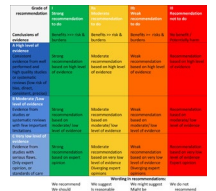
Quality of studies assessed using **Cochrane Risk of Bias** tool for RCTs and **AMSTAR** for Systematic Reviews.



Search terms determined by guideline panel based on **PICO**



Recommendations were developed using **GRADE** Methodology



References were screened and relevant data extracted and analysed using **Distiller SR**



The guideline recommendations were developed and reported in accordance with **AGREE** checklist



PICO

In patients with select clinical indications, does **intravenous albumin** improve **pre-specified outcomes** when compared to comparator therapies?*

P*

- Hypovolemia
- Sepsis
- Hypoalbuminemia
- Thermal injuries
- Acute respiratory distress syndrome
- Cirrhosis
- Intradialytic hypotension
- Cardiovascular surgery

I

Intravenous albumin

C

- Synthetic colloids
- Crystalloids

O

- Mortality
- Kernicterus
- Acute neurological impairment
- Chronic neurological impairment
- Need for exchange transfusion
- Need for top-up transfusion
- Bilirubin level
- Anemia
- Length of hospital stay

Literature Review

Identification of studies from MEDLINE, EMBASE, Cochrane, National Health Service Economic Evaluation Database, Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, Ovid MEDLINE(R), Ovid MEDLINE(R) epub ahead of print and in-process and other non-indexed citations
From Inception- November 2022

6783
total records identified
6186
records excluded after screening

Limitation of the search to the English language

Lack of comparative dosing strategies leaves uncertainty in choice between 4-5% and 20-25% albumin formulations

Studies often did not report adverse reactions

The guideline is limited to common uses of albumin and cannot address every possible patient scenario

597
full-text articles

54
studies

Quality Assessment



Statements

TABLE 1] The 14 Recommendations From the Panel, Ordered by Strength of the Recommendations

<p>Moderate Certainty of Evidence</p> <p>Recommendation 1: In critically ill adult patients (excluding patients with thermal injuries and ARDS), intravenous albumin is not suggested for first-line volume replacement or to increase serum albumin levels (Conditional Recommendation, Moderate Certainty of Evidence of Effect).</p> <p>Recommendation 8: In adult patients undergoing cardiovascular surgery, intravenous albumin is not suggested for priming the cardiovascular bypass circuit or for volume replacement (Conditional Recommendation, Moderate Certainty of Evidence of Effect).</p>
<p>Low Certainty of Evidence</p> <p>Recommendation 4: In pediatric patients with infection and hypoperfusion, intravenous albumin is not recommended to reduce mortality (Strong Recommendation, Low Certainty of Evidence of Effect).</p> <p>Recommendation 11: In patients with cirrhosis and spontaneous bacterial peritonitis, intravenous albumin is suggested to reduce mortality (Conditional Recommendation, Low Certainty of Evidence of Effect).</p> <p>Recommendation 12: In patients with cirrhosis and extraperitoneal infections, intravenous albumin is not suggested to reduce mortality or kidney failure (Conditional Recommendation, Low Certainty of Evidence of Effect).</p> <p>Recommendation 13: In hospitalized patients with decompensated cirrhosis with hypoalbuminemia (< 30 g/L), repeated intravenous albumin to increase albumin levels to > 30 g/L is not suggested to reduce infection, kidney dysfunction, or death (Conditional Recommendation, Low Certainty of Evidence of Effect).</p> <p>Recommendation 14: In outpatients with cirrhosis and uncomplicated ascites despite diuretic therapy, intravenous albumin is not routinely suggested to reduce complications associated with cirrhosis (Conditional Recommendation, Low Certainty of Evidence of Effect).</p>
<p>Very low Certainty of Evidence</p> <p>Recommendation 2: In critically ill adult patients with thermal injuries or ARDS, intravenous albumin is not suggested for volume replacement or to increase serum albumin level (Conditional Recommendation, Very Low Certainty of Evidence of Effect).</p> <p>Recommendation 3: In critically ill adult patients, intravenous albumin in conjunction with diuretics is not suggested for removal of extravascular fluid (Conditional Recommendation, Very Low Certainty of Evidence of Effect).</p> <p>Recommendation 5: In preterm neonates (≤ 36 wk) with respiratory distress and low serum albumin levels, intravenous albumin is not suggested to improve respiratory function (Conditional Recommendation, Very Low Certainty of Evidence of Effect).</p> <p>Recommendation 6: In preterm neonates (≤ 32 wk or $\leq 1,500$ g) with or without hypoperfusion, intravenous albumin is not suggested for volume replacement (Conditional Recommendation, Very Low Certainty of Evidence of Effect).</p> <p>Recommendation 7: In patients undergoing kidney replacement therapy, intravenous albumin is not suggested for the prevention or treatment of intradialytic hypotension or for improving ultrafiltration (Conditional Recommendation, Very Low Certainty of Evidence of Effect).</p> <p>Recommendation 9: In pediatric patients undergoing cardiovascular surgery, intravenous albumin is not suggested for priming the cardiovascular bypass circuit or for volume replacement (Conditional Recommendation, Very Low Certainty of Evidence of Effect).</p> <p>Recommendation 10: In patients with cirrhosis and ascites undergoing large-volume paracentesis (> 5 L), intravenous albumin is suggested to prevent paracentesis-induced circulatory dysfunction (Conditional Recommendation, Very Low Certainty of Evidence of Effect).</p>



[Link to Guidelines](#)



Cirrhosis
N=5

**Critical
Care**
N=3

**Pediatric &
Neonatal**
N=3

**CV
Surgery**
N=2

Renal
N=1



Cirrhosis
N=5

**Critical
Care**
N=3

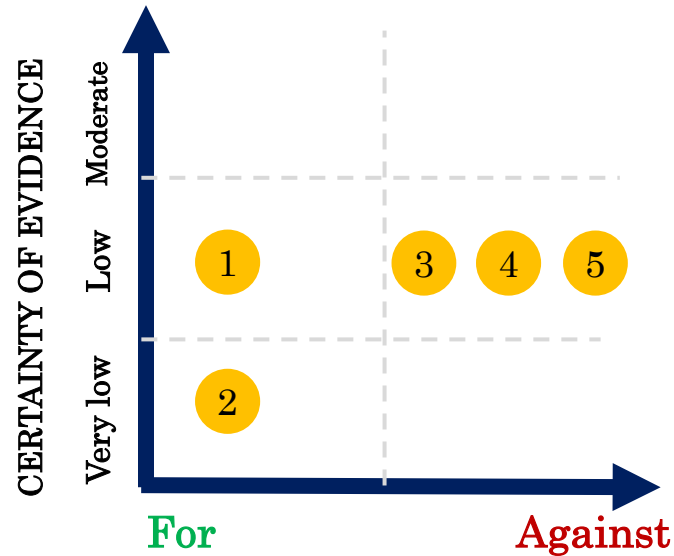
**Pediatric &
Neonatal**
N=3

**CV
Surgery**
N=2

Renal
N=1



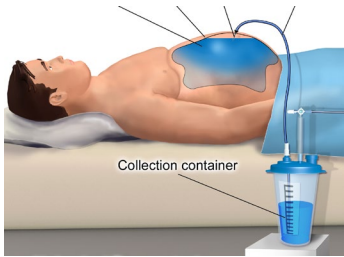
Cirrhosis N=5



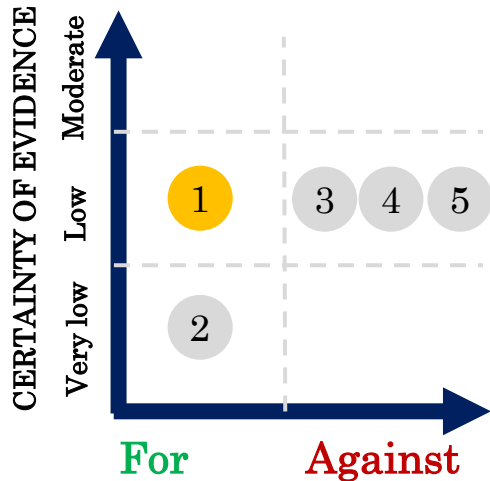
1. In patients with cirrhosis and ascites undergoing large-volume paracentesis (> 5 L), intravenous albumin is suggested to prevent paracentesis-induced circulatory dysfunction
2. In patients with cirrhosis and spontaneous bacterial peritonitis, intravenous albumin is suggested to reduce mortality
3. In patients with cirrhosis and extraperitoneal infections, intravenous albumin is not suggested to reduce mortality or kidney failure
4. In hospitalized patients with decompensated cirrhosis with hypoalbuminemia (< 30 g/L), repeated intravenous albumin to increase albumin levels to > 30 g/L is not suggested to reduce infection, kidney dysfunction, or death
5. In outpatients with cirrhosis and uncomplicated ascites despite diuretic therapy, intravenous albumin is not routinely suggested to reduce complications associated with cirrhosis



1. In patients with cirrhosis and ascites undergoing large-volume paracentesis (> 5 L), intravenous albumin is suggested to prevent paracentesis-induced circulatory dysfunction



Recommended dose:
Alb 20-25%, 6-8 g/L of fluid removed



Cochrane Database of Systematic Reviews

Plasma expanders for people with cirrhosis and large ascites treated with abdominal paracentesis (Review)

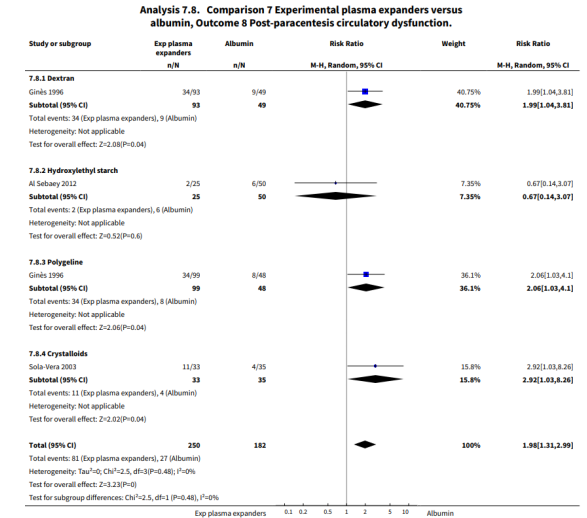
Simonetti RG, Perricone G, Nikolova D, Bjelakovic G, Gluud C
Cochrane Database Syst Rev. 2019 Jun 28;6(6):CD004039.

27 RCTs (N = 1,592) examining plasma volume expanders cirrhosis + paracentesis

Included patients having large-volume paracentesis (> 5 L)

Compared with no plasma expander, hyperoncotic albumin (20-25%) showed

- **No effect** of using hyperoncotic (20%-25%) albumin on
 - **Mortality** (RR, 0.52; 95% CI, 0.06-4.83)
 - **Kidney impairment** (RR, 0.32; 95% CI, 0.02-5.88),
 - **Recurrence of ascites** (RR, 1.3; 95% CI, 0.49-3.42)
- **Benefit for paracentesis-induced circulatory dysfunction** (RR, 1.98; 95% CI, 1.31-2.99)



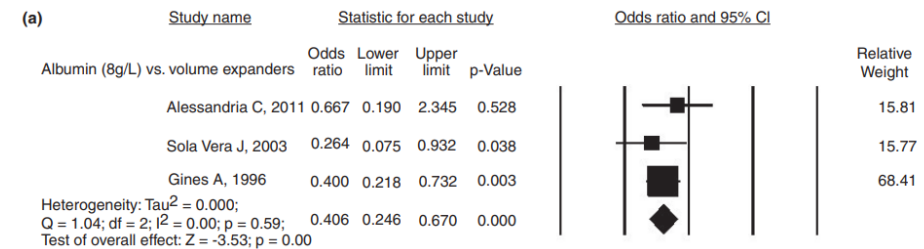
Prevention of paracentesis-induced circulatory dysfunction—A systematic review and network meta-analysis

Anand V. Kulkarni¹ | Pramod Kumar¹ | Siddharth Singh² | Mithun Sharma¹ | Rupiyoti Talukdar³ | Vivekananda H.V. Murthy⁴ | Virendra Singh⁵ | Nageshwar D Reddy³ | Nagaraja Padaki Rao¹

A 2020 systematic review focused on the impact of different therapies (albumin, other fluids, vasoactive drugs) on the rate of postparacentesis circulatory dysfunction

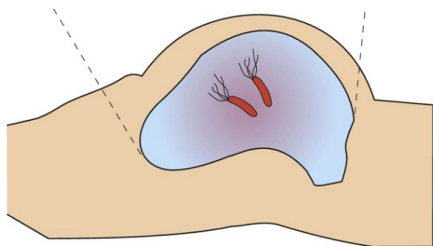
Included (n=9 RCTs, 620 patients)

Found albumin at a dose of 8 g/L was found to be superior to other volume expanders for preventing post-paracentesis circulatory dysfunction



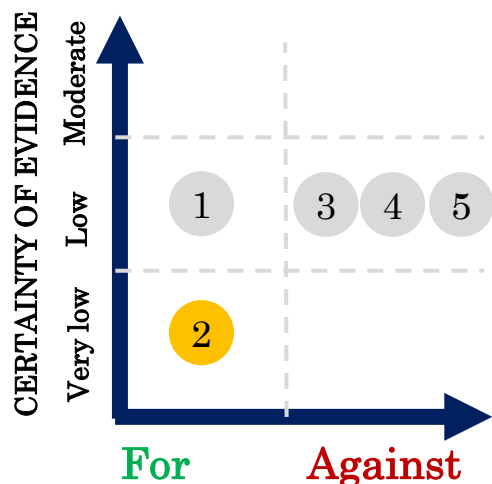


2. In patients with cirrhosis and spontaneous bacterial peritonitis, intravenous albumin is suggested to reduce mortality



Recommended dose:

Alb 20-25%, Day 1: 1.5 g/kg, Day 3: 1.0 g/kg*



Giacomo Zaccherini
Manuel Tufoni
Mauro Bernardi
Department of Medical and Surgical
Sciences, Alma Mater Studiorum -
University of Bologna, Bologna 40138,
Italy

Albumin Administration is Efficacious in the Management of Patients with Cirrhosis: A Systematic Review of the Literature

Two SRs identified 5 unblinded RCTs
Trials used variable doses and duration of hyperoncotic albumin

SYSTEMATIC REVIEWS AND META-ANALYSES

Fasiha Kanwal, Section Editor

Albumin Infusion Improves Outcomes of Patients With Spontaneous Bacterial Peritonitis: A Meta-analysis of Randomized Trials

Albumin reduced:

- Rate of kidney impairment (OR, 0.21; 95% CI, 0.11-0.42)
- Mortality (OR, 0.34; 95% CI, 0.19-0.60)

Effect of Intravenous Albumin on Renal Impairment and Mortality in Patients with Cirrhosis and Spontaneous Bacterial Peritonitis

Authors: Pau Sort, M.D., Miquel Navasa, M.D., Vicente Arroyo, M.D., Xavier Aldeguer, M.D., Ramon Planas, M.D., Luis Ruiz-del-Arbol, M.D., Lluís Castells, M.D., Victor Vargas, M.D., Germán Soriano, M.D., Mónica Guevara, M.D., Pere Ginès, M.D., and Joan Rodés, M.D. [Author Info & Affiliations](#)

Published August 5, 1999 | N Engl J Med 1999;341:403-409 | DOI: 10.1056/NEJM199908053410603

Largest RCT, randomized 126 patients to albumin + abx, or abx alone

Patients treated with albumin showed

- Lower kidney impairment (10% vs 33%; P = .002)
- Lower in-hospital mortality (10% vs 29%; P = .01)

Efficacy of Albumin Treatment for Patients with Cirrhosis and Infections Unrelated to Spontaneous Bacterial Peritonitis

Javier Fernández,^{1,2} Paolo Angeli,^{3,4} Jonel Trebicka,^{5,6} Manuela Merli,⁷ Thierry Gustot,⁸ Carlo Alessandria,⁹ Niels Kristian Aagaard,¹⁰ Andrea de Gottardi,¹¹ Tania M. Welzel,¹² Alexander Gerbes,¹³ German Soriano,¹⁴ Victor Vargas,¹⁵ Agustín Albillos,¹⁶ Francesco Salerno,¹⁷ Francois Durand,¹⁸ Rafael Bañares,¹⁹ Rudolf Stauber,²⁰ Verónica Prado,²¹ Mireya Arteaga,²² María Hernández-Tejero,²³ Fátima Aziz,²⁴ Filippo Morando,²⁵ Christian Jansen,²⁶ Barbara Lattanzi,²⁷ Christophe Moreno,²⁸ Daniela Campion,²⁹ Henning Gronbaek,³⁰ Rita Garcia,³¹ Cristina Sánchez,³² Elisabet García,³³ Alex Amorós,³⁴ Marco Pavesi,³⁵ Joan Clària,³⁶ Richard Moreau,^{37,38,39} and Vicente Arroyo⁴⁰

Clinical Gastroenterology and Hepatology 2020;18:963-973

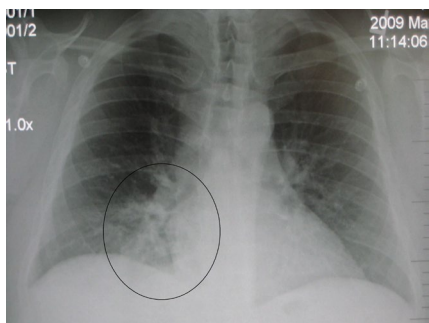
Second largest RCT, randomized 118 patients to albumin (plus antibiotics) or antibiotics alone

No effect on in-hospital mortality (13% vs 11%; P = .66)

Benefit seen for acute-on-chronic liver failure and new infections



3. In patients with cirrhosis and extraperitoneal infections, intravenous albumin is not suggested to reduce mortality or kidney failure



Efficacy and Safety of IV albumin for non-spontaneous bacterial peritonitis infection among patients with cirrhosis: A systematic review and meta-analysis

Yu-Jun WONG^a, Tian-Yu QIU^a, Yew-Chong TAM^b, Babu P MOHAN^{c,d}, Juan-F GALLEGOS-OROZCO^d, Douglas G ADLER^{d,*}

2020 systematic review and meta-analysis of RCTs (3 RCTs, n=406)

- **No effect** on mortality or kidney impairment
- **Higher rates of pulmonary edema** with albumin (three studies [N = 406]; OR, 5.17; 95% CI, 1.62-16.47)
- **Higher resolution** of acute on chronic liver failure (OR=0.11, 95%CI: 0.02-0.69, p=0.02)

Comparison of 5% human albumin and normal saline for fluid resuscitation in sepsis induced hypotension among patients with cirrhosis (FRISC study): a randomized controlled trial

Cyriac Abby Philips¹ · Rakhi Maiwall¹ · Manoj Kumar Sharma¹ · Ankur Jindal¹ · Ashok Kumar Choudhury¹ · Guresh Kumar² · Ankit Bhardwaj² · Lalita Gouri Mitra³ · Prashant Mohan Agarwal³ · Shiv Kumar Sarin^{1,2}

n = 308

- **Similar survival** at 7 days in the albumin-treated patients (saline, 39.0% vs albumin, 43.5%; P = .42, Fisher exact test)
- **Higher reversal of hypotension** in patients receiving 5% albumin at 1 hr and 3 hr transfusion

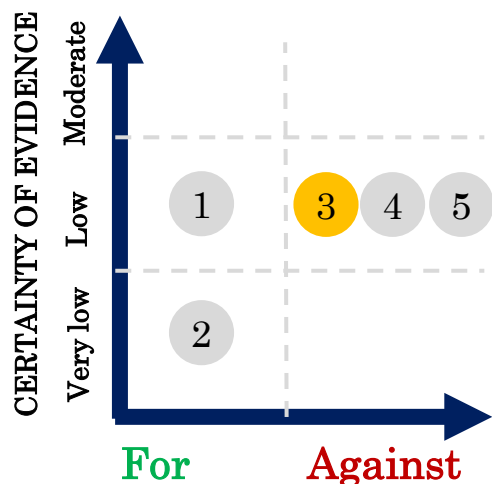
Research Article
Cirrhosis and Liver Failure

JOURNAL
OF HEPATOLOGY

A randomized-controlled trial comparing 20% albumin to plasmalyte in patients with cirrhosis and sepsis-induced hypotension [ALPS trial]

n = 100

- **No effect** on initiation of dialysis, length of stay, or mortality at 28 days
- **Superior** to crystalloid for reversal of hypotension without initiation of vasopressors at 3 h (22% vs 62%; P < .001)





4. In hospitalized patients with decompensated cirrhosis with hypoalbuminemia (< 30 g/L), repeated intravenous albumin to increase albumin levels to > 30 g/L is not suggested to reduce infection, kidney dysfunction, or death

ATTIRE Study

A Randomized Trial of Albumin Infusions in Hospitalized Patients with Cirrhosis

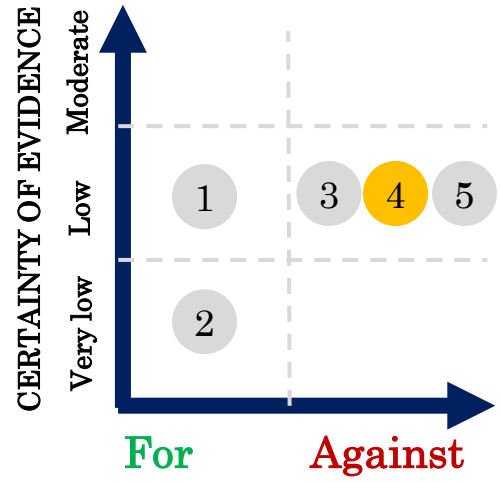
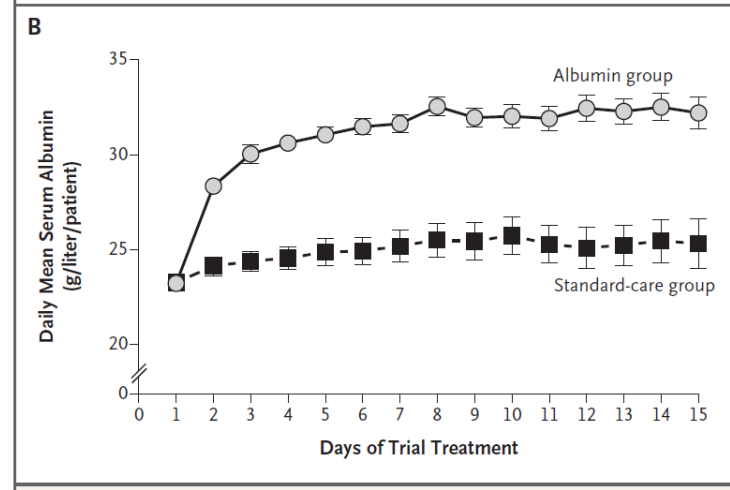
Authors: Louise China, Ph.D., Nick Freemantle, Ph.D., Ewan Forrest, M.D., Yiannis Kallis, Ph.D., Stephen D. Ryder, D.M., Gavin Wright, Ph.D., Andrew J. Portal, M.D., Natalia Becares Salles, Ph.D., Derek W. Gilroy, Ph.D., and Alastair O'Brien, Ph.D., for the ATTIRE Trial Investigators* [Author Info & Affiliations](#)

Published March 3, 2021 | N Engl J Med 2021;384:808-817 | DOI: 10.1056/NEJMoa2022166 | [VOL. 384 NO. 9](#)



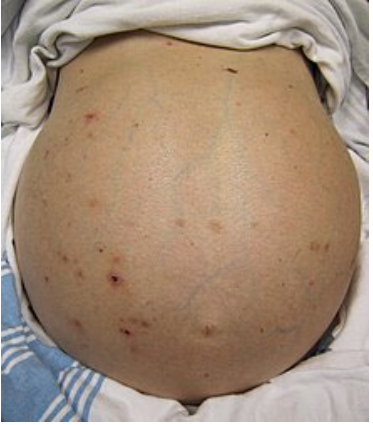
- Patients with hypoalbuminemia included (n=777)
- Randomly received either targeted 20% human albumin solution for up to 14 days or until discharge, whichever came first, or standard care
- **No difference** was found in the primary end point (composite of new infections, kidney dysfunction, or death between days 3 and 15) (OR, 0.98; 95% CI, 0.71-1.33)
- **More severe or life-threatening serious adverse events** were reported in the albumin-treated patients, primarily a numerical increase in pulmonary edema.

Median Albumin given: 200 g





5. In outpatients with cirrhosis and uncomplicated ascites despite diuretic therapy, intravenous albumin is not routinely suggested to reduce complications associated with cirrhosis



Midodrine and albumin for prevention of complications in patients with cirrhosis awaiting liver transplantation. A randomized placebo-controlled trial

J Hepatol. 2018;69(6):1250-1259.

- Randomized 440 patients with cirrhosis and uncomplicated, persistent ascites despite diuretic therapy
- Albumin (40 g twice weekly for 2 weeks and then 40 g weekly for up to 18 months) or no albumin.
- Patients randomized to albumin experienced
 - Longer time to first paracentesis; required fewer paracenteses
 - Lower hepatic encephalopathy, hepatorenal syndrome, spontaneous bacterial peritonitis, nonperitonitis infections, hyponatremia, or kidney dysfunction; experienced fewer days in hospital; lower all-cause mortality

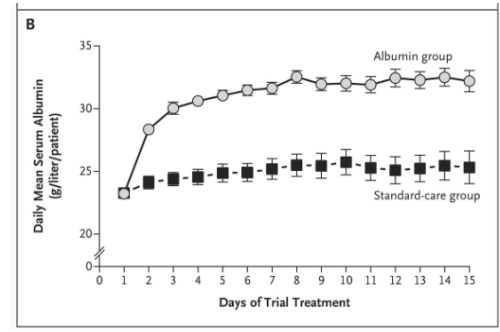
Limitation—Performance Bias: albumin-treated patients underwent weekly health care interactions and the control group did not (!!)

A Randomized Trial of Albumin Infusions in Hospitalized Patients with Cirrhosis

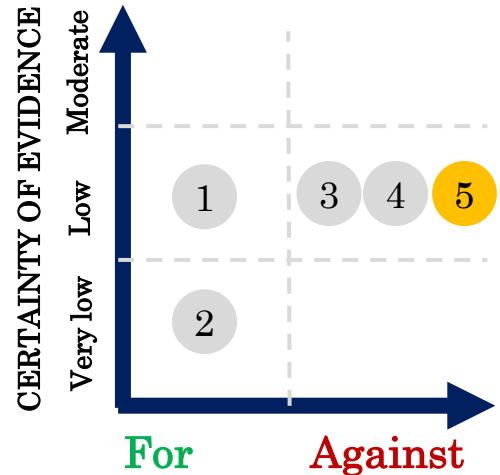


- N = 196 outpatients, ascites awaiting liver transplantation
- RCT: Oral midodrine and albumin or saline placebo

The dose of albumin given as part of the intervention was lower (40 g every 15 days).



No difference in patient outcomes (end point was new infection, kidney dysfunction, or death, days 3-15)





Cirrhosis
N=5

**Critical
Care**
N=3

**Pediatric &
Neonatal**
N=3

**CV
Surgery**
N=2

Renal
N=1

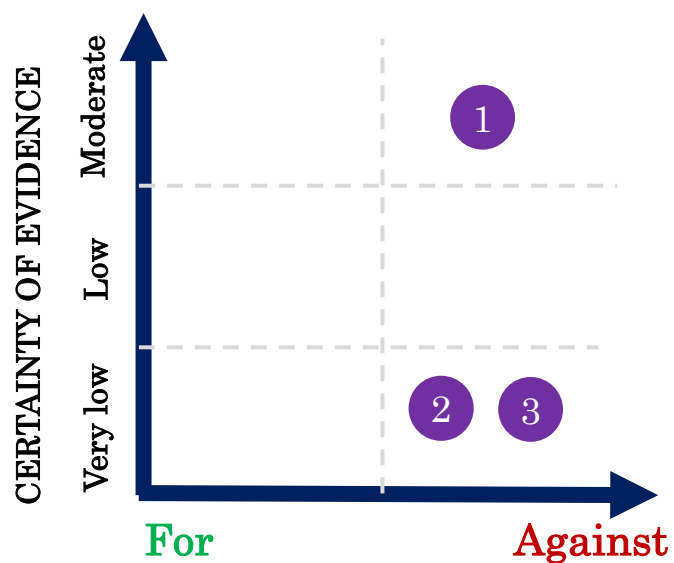


Critical Care N=3

1. In critically ill adult patients (excluding patients with thermal injuries and ARDS), intravenous albumin is not suggested for first-line volume replacement or to increase serum albumin levels

2. In critically ill adult patients with thermal injuries or ARDS, intravenous albumin is not suggested for volume replacement or to increase serum albumin level

3. In critically ill adult patients, intravenous albumin in conjunction with diuretics is not suggested for removal of extravascular fluid





1 In critically ill adult patients (excluding patients with thermal injuries and ARDS), intravenous albumin is not suggested for first-line volume replacement or to increase serum albumin levels



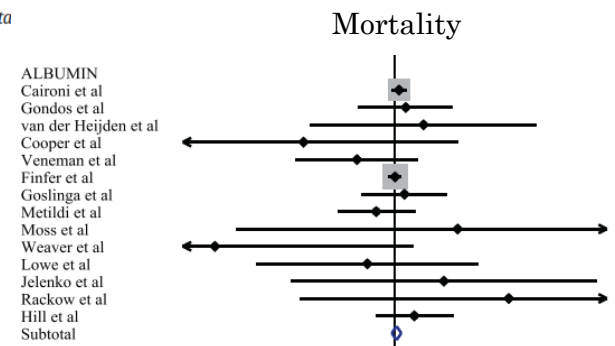
Crystalloids vs. colloids for fluid resuscitation in the Intensive Care Unit: A systematic review and meta-analysis

Greg S. Martin ^{a,*}, Paul Bassett ^b

^a Division of Pulmonary, Allergy, Critical Care and Sleep Medicine, Department of Medicine, Emory University School of Medicine, Grady Memorial Hospital, Atlanta
^b Meridian HealthComms, Plumley Moor Road, Plumley, UK

A systematic review from 2019 identified 55 RCTs comparing crystalloid with colloids in critical care. Data on mortality were available for 26,329 patients from 46 studies.

- **Better** peak mean arterial pressure with albumin
- **No mortality benefit** was found when crystalloid was compared with albumin (relative risk [RR] 1.02; 95% CI, 0.96-1.10)



ORIGINAL ARTICLE

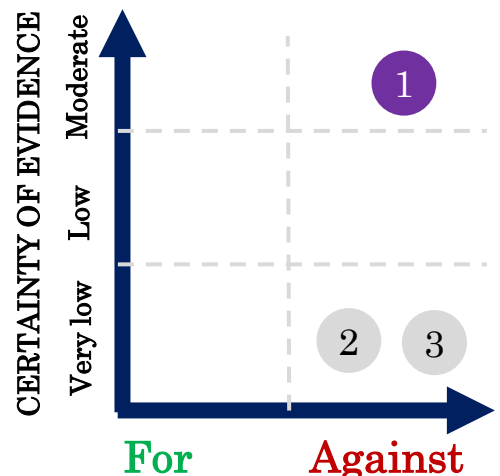
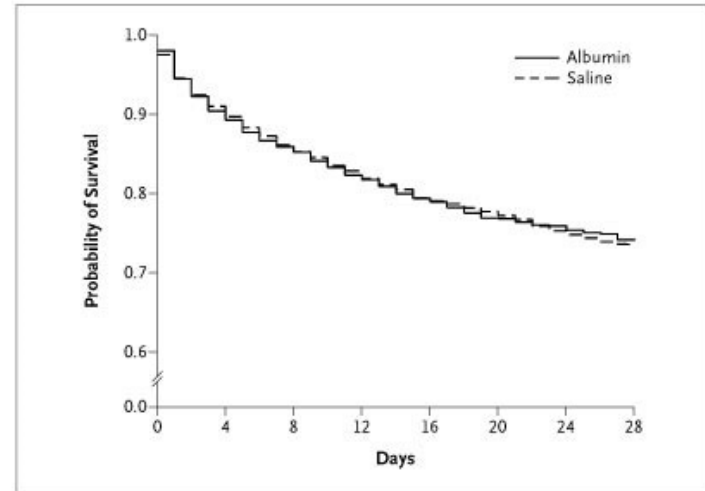
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A Comparison of Albumin and Saline for Fluid Resuscitation in the Intensive Care Unit

Author: The SAFE Study Investigators* Author Info & Affiliations

Published May 27, 2004 | N Engl J Med 2004;350:2247-2256 | DOI: 10.1056/NEJMoa040232 | VOL. 350 NO. 22

- 6,997 patients receiving critical care (including a mix of medical and surgical patients)
- Compared 4% albumin with 0.9% normal saline.
- **No differences were found in outcomes**, including 28-day mortality (RR, 0.99; 95% CI, 0.91-1.09)
- **Subgroup analysis found that patients** with traumatic brain injury showed a higher mortality rate (RR, 1.62; 95% CI, 1.12- 2.34)





2. In critically ill adult patients with thermal injuries or ARDS, intravenous albumin is not suggested for volume replacement or to increase serum albumin level



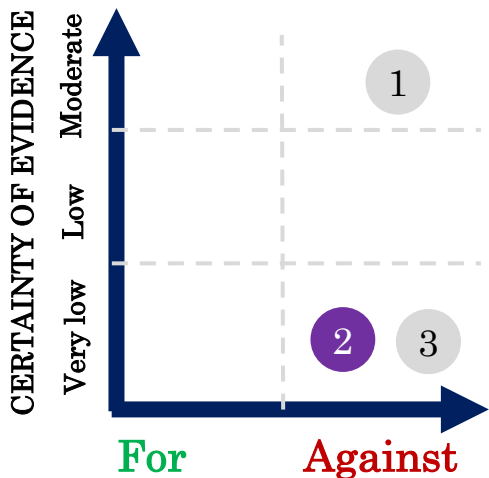
Albumin in Burn Shock Resuscitation: A Meta-Analysis of Controlled Clinical Studies

Roberta J. Navickis, PhD,* David G. Greenhalgh, MD, FACS,††
Mahlon M. Wilkes, PhD*

Included 4 RCTs and 4 observational studies

Overall, albumin infusion during the first 24 hours showed no significant overall effect on mortality

After those exclusions, albumin infusion was associated with reduced mortality. The pooled odds ratio was 0.34 with a 95% confidence interval of 0.19 to 0.58 (P < .001).



Study	Albumin		Control		
	Events	Total	Events	Total	
Randomized					
Recinos et al (1975) ³³	2	9	5	9	
Jelenko et al (1979) ³⁴	1	7	3	12	
Goodwin et al (1983) ³⁵	11	25	3	25	
Cooper et al (2006) ³⁶	3	19	1	23	
<i>Subtotal</i>	17	60	12	69	
Nonrandomized					
Cochran et al (2007) ³⁷	19	101	11	101	
Ennis et al (2008) ³⁹	10	56	19	62	
Park et al (2012) ⁴⁰	5	61	26	98	
<i>Subtotal</i>	34	218	56	261	
Total	51	278	68	330	

Heterogeneity: I^2 , 66.0% (CI, 23.8-84.8%); $P = .007$

Favors Albumin

Favors Control

Randomized

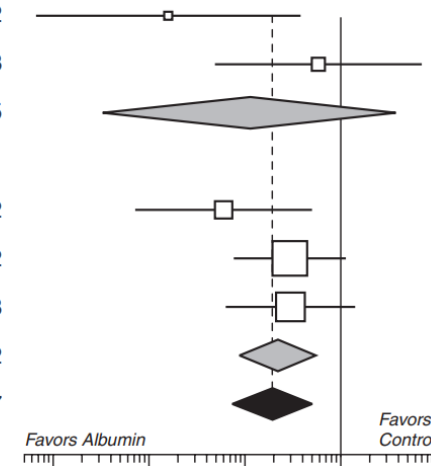
Jelenko et al (1979) ³⁴	0	7	10	12
Cooper et al (2006) ³⁶	1	19	2	23
<i>Subtotal</i>	1	26	12	35

Nonrandomized

Dulhunty et al (2008) ³⁸	—†	68	—†	12
Ennis et al (2008) ³⁹	3	56	10	62
Park et al (2012) ⁴⁰	2	61	10	98
<i>Subtotal</i>	5	185	20	172

Total 6 211 32 207

Heterogeneity: I^2 , 19.3% (CI, 0.0-83.2%); $P = .29$



3. In critically ill adult patients, intravenous albumin in conjunction with diuretics is not suggested for removal of extravascular fluid



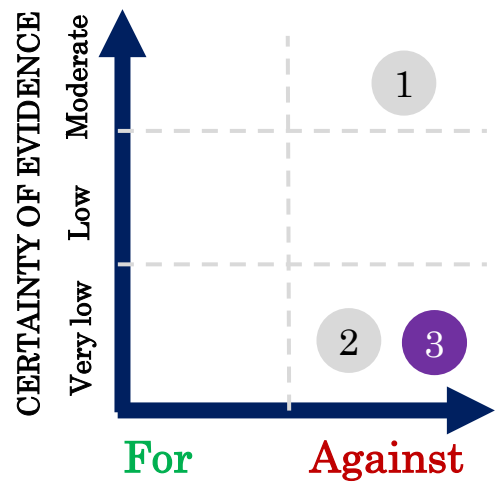
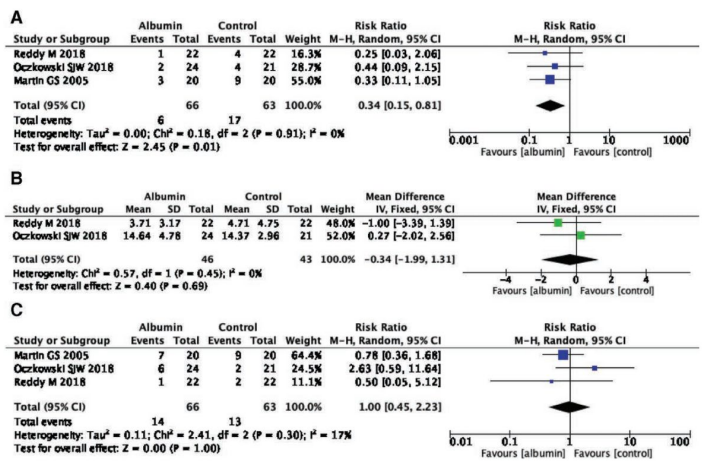
Efficacy of albumin with diuretics in mechanically ventilated patients with hypoalbuminemia

A systematic review and meta-analysis

Yuki Itagaki, MD^{a,b,c,*}, Naofumi Yoshida, MD, PhD^{c,d}, Masahiro Banno, MD, PhD^{e,f}, Ryo Momosaki, MD, MPH, PhD^{c,g}, Kohei Yamada, MD, MPH^{c,h}, Mineji Hayakawa, MD, PhD^b

2022 SR/MA identified 3 RCTs (n=129)

- Trials of albumin + diuretics vs. placebo + diuretics
- Albumin reduced hypotensive episodes
- No effect on mortality, days of mechanical ventilation



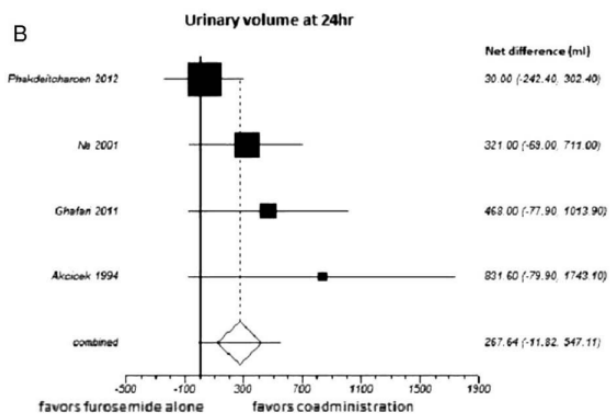
Renal/Metabolic

Co-administration of furosemide with albumin for overcoming diuretic resistance in patients with hypoalbuminemia: A meta-analysis

Georgios D. Kitsios, MD PhD^{a,b,*}, Paolo Mascari, MD PharmD^a, Riad Ettunsi, MD MSc^a, Anthony W. Gray, MD^a

Included 10 RCTs of albumin with furosemide, compared with furosemide alone (N = 343).

- Urine output was higher at 6h in the patients receiving albumin-furosemide, no difference was found in urine output at 24h.





Cirrhosis
N=5

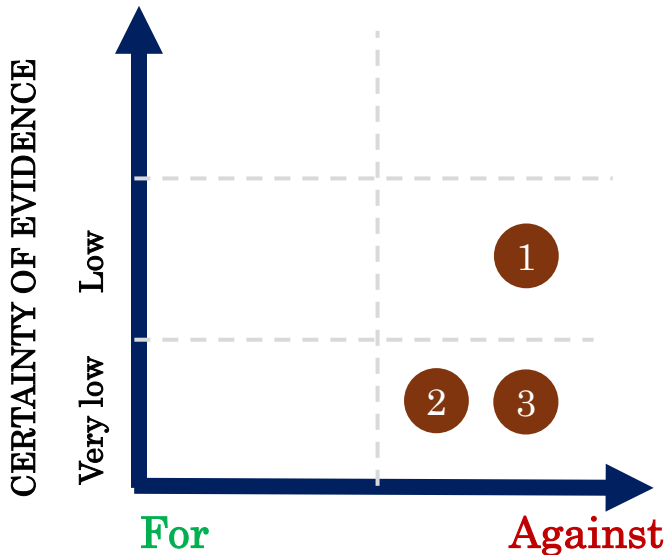
**Critical
Care**
N=3

**Pediatric &
Neonatal**
N=3

**CV
Surgery**
N=2

Renal
N=1

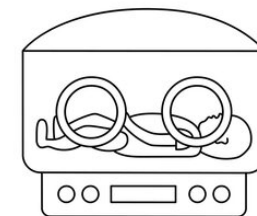
**Pediatric & Neonatal
N=3**



1. In pediatric patients with infection and hypoperfusion, intravenous albumin is not recommended to reduce mortality (Strong Recommendation, Low Certainty of Evidence of Effect).



2. In preterm neonates (≤ 36 weeks) with low serum albumin levels and respiratory distress, intravenous albumin is not suggested to improve respiratory function



3. In preterm neonates (≤ 32 weeks or $\leq 1,500$ g) with or without hypoperfusion, intravenous albumin is not suggested for volume replacement

1 In pediatric patients with infection and hypoperfusion, intravenous albumin is not recommended to reduce mortality (Strong Recommendation, Low Certainty of Evidence of Effect).



Mortality after Fluid Bolus in Children with Shock Due to Sepsis or Severe Infection: A Systematic Review and Meta-Analysis

Nathan Ford, Sally Hargreaves, Leslie Shanks

Included n = 13 studies

Better mortality outcomes in no bolus (albumin or saline) arms at 48 hours for children with general septic shock (RR 0.69; 95%CI 0.54–0.89), and children with malaria (RR 0.64; 95%CI 0.45–0.91) when compared to giving any bolus.

ORIGINAL ARTICLE

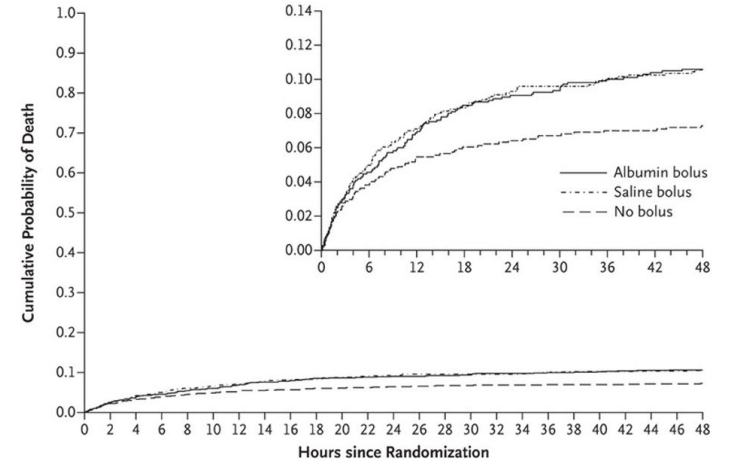
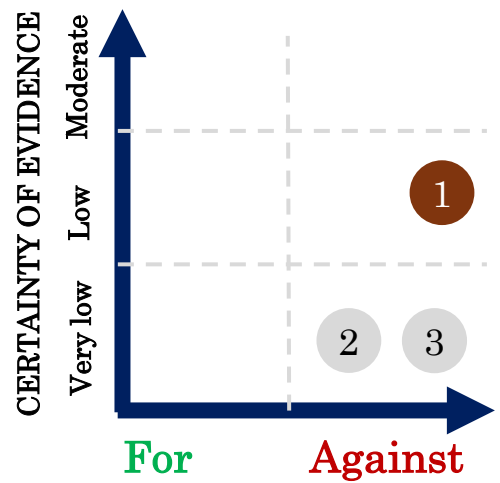


Mortality after Fluid Bolus in African Children with Severe Infection

Authors: Kathryn Maitland, M.B., B.S., Ph.D., Sarah Kiguli, M.B., Ch.B., M.Med., Robert O. Opoka, M.B., Ch.B., M.Med., Charles Engoru, M.B., Ch.B., M.Med., Peter Olupot-Olupot, M.B., Ch.B., Samuel O. Akech, M.B., Ch.B., Richard Nyeko, M.B., Ch.B., M.Med., [et al.](#), for the FEAST Trial Group* [Author Info & Affiliations](#)

Children (n= 3141) with febrile illnesses randomly assigned to receive boluses of 5% albumin or 0.9% saline (20-40 ml/kg) or nothing

The 4-week mortality was 12.2%, 12.0%, and 8.7% in the three groups, respectively (P=0.004 for the comparison of bolus with control). Trial stopped prematurely





Early volume expansion for prevention of morbidity and mortality in very preterm infants (Review)

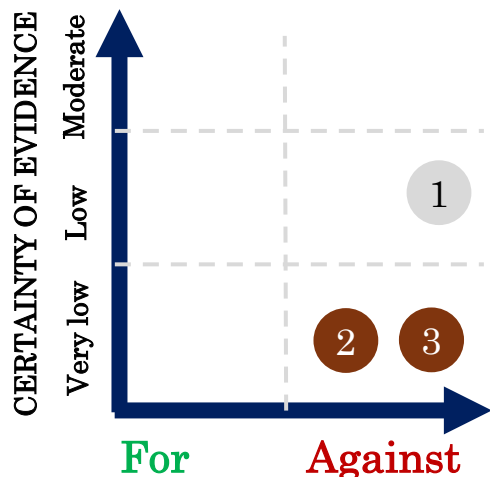
Albumin infusion for low serum albumin in preterm newborn infants (Review)

Study	Participants	Intervention	Comparator	Outcome (Effect Measure)	Results
Cochrane SR 1 (2004)	64 preterm neonates (≤ 36 weeks' gestation)	Albumin	No treatment	Mortality (RR not significant)	No difference in mortality or other outcomes observed.
Cochrane SR 2 (2004)	Variable preterm neonates (≤ 32 weeks or $\leq 1,500$ g)	Various fluids (including albumin)	Normal saline, plasma, no treatment	Mortality (RR)	<ul style="list-style-type: none"> - Albumin vs normal saline (N = 102): RR 1.02 (95% CI 0.50-2.06), no difference. - Albumin vs no treatment (N = 25): RR 0.92 (95% CI 0.23-3.72), no difference. - Albumin vs plasma (N = 20): No difference in duration of ventilation (mortality not reported).

2 In preterm neonates (≤ 36 weeks) with low serum albumin levels and respiratory distress, intravenous albumin is not suggested to improve respiratory function



3 In preterm neonates (≤ 32 weeks or $\leq 1,500$ g) with or without hypoperfusion, intravenous albumin is not suggested for volume replacement



Journal of Perinatology: Albumin versus normal saline for dehydrated term infants with metabolic acidosis due to acute diarrhea

JJ Han, HE Yim, JH Lee, YK Kim, GY Jang, BM Choi, KH Yoo & YS Hong

Single RCT	33 term infants with dehydration, metabolic acidosis, diarrhea	5% albumin (10 mL/kg)	Normal saline (10 mL/kg)	Various outcomes	No differences in outcomes observed.
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Cirrhosis
N=5

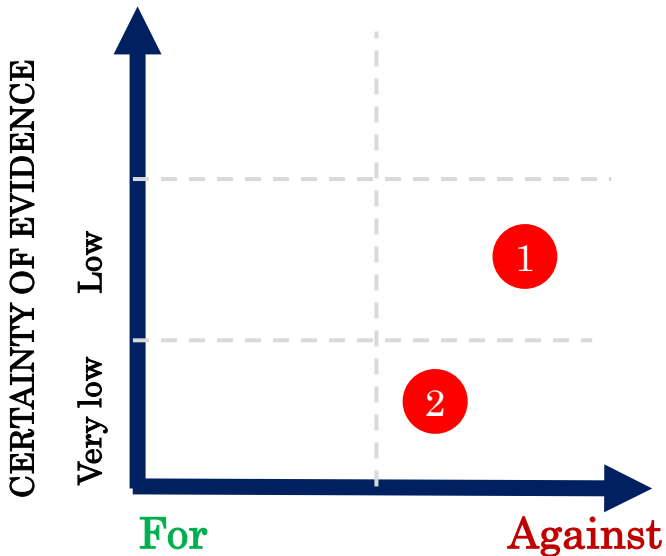
**Critical
Care**
N=3

**Pediatric &
Neonatal**
N=3

**CV
Surgery**
N=2

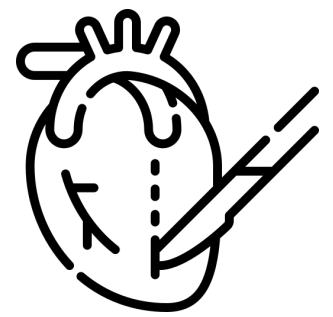
Renal
N=1

CV Surgery
N=2



1. In adult patients undergoing cardiovascular surgery, intravenous albumin is not suggested for priming the cardiovascular bypass circuit or volume replacement

2. In pediatric patients undergoing cardiovascular surgery, intravenous albumin is not suggested for priming the cardiovascular bypass circuit or volume replacement





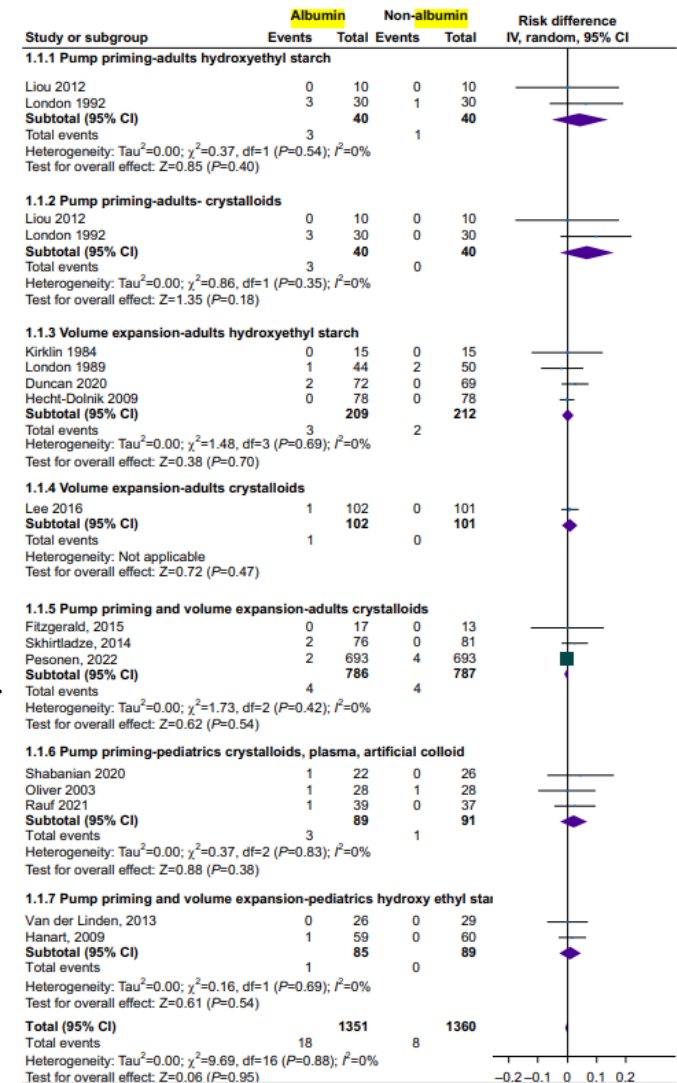
CARDIOVASCULAR

Intravenous albumin in cardiac and vascular surgery: a systematic review and meta-analysis

Nikolaos J. Skubas^{1,*}, Jeannie Callum², Aarti Bathla³, Homa Keshavarz⁸, Dean Fergusson⁴, Bovey Wu⁵, Simon Stanworth⁶, Nadine Shehata⁷ on behalf of the International Collaboration for Transfusion Medicine Guidelines

¹Department of Cardiothoracic Anaesthesiology, Anaesthesiology Institute, Cleveland Clinic, and Cleveland Clinic, Lerner College of Medicine of Case Western Reserve University, Cleveland, OH, USA, ²Department of Pathology and Molecular Medicine, Queen's University and Kingston Health Sciences Centre, Kingston, ON, Canada, ³Canadian Blood Services, Toronto, Canada, ⁴Ottawa Hospital Research Institute, Ottawa, ON, Canada, ⁵Department of Internal Medicine, School of Medicine, Loma Linda University, Loma Linda, CA, USA, ⁶NHS Blood and Transplant, Bristol, UK, ⁷Departments of Medicine, Laboratory Medicine and Pathobiology, Institute of Health Policy Management and Evaluation, University of Toronto, Division of Hematology, Mount Sinai Hospital, Toronto, ON, Canada and ⁸Canadian Blood Services, Ottawa, Canada

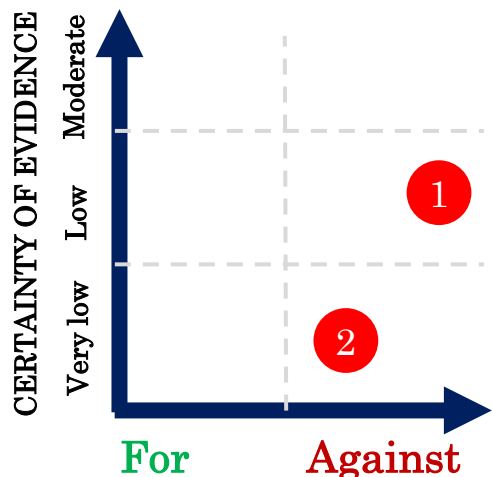
- 42 randomized controlled trials comparing intravenous albumin with synthetic colloids and crystalloids in cardiovascular surgery.
- Primary outcome: all-cause mortality.
- Secondary outcomes included renal failure, blood loss, duration of hospital or ICU stay, cardiac index, and blood component use.
- Subgroups of age, comparator fluid, and intended use (priming, volume replacement, or both).
- Results
 - No significant difference in mortality between albumin and comparator fluids.
 - No difference in rates of kidney failure, blood loss, hospital length of stay, cardiac index
 - Albumin resulted in smaller fluid balance and higher albumin concentrations compared to other fluids.



1. In adult patients undergoing cardiovascular surgery, intravenous albumin is not suggested for priming the cardiovascular bypass circuit or volume replacement



2. In pediatric patients undergoing cardiovascular surgery, intravenous albumin is not suggested for priming the cardiovascular bypass circuit or volume replacement





Cirrhosis
N=5

**Critical
Care**
N=3

**Pediatric &
Neonatal**
N=3

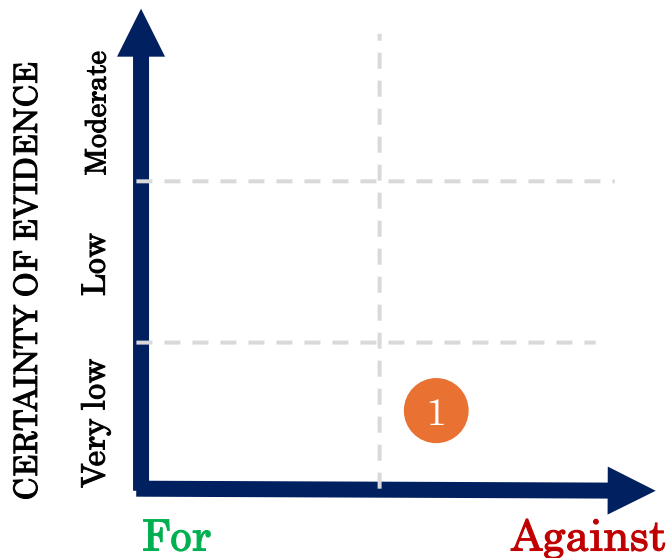
**CV
Surgery**
N=2

Renal
N=1



Renal
N=1

1. In patients undergoing kidney replacement therapy, intravenous albumin is not suggested for prevention or treatment of intradialytic hypotension or for improving ultrafiltration





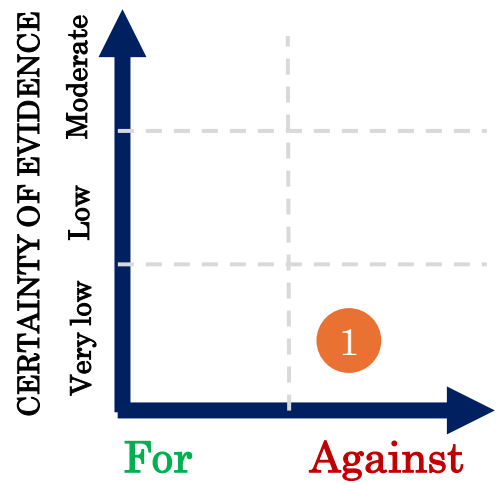
1 In patients undergoing kidney replacement therapy, intravenous albumin is not suggested for prevention or treatment of intradialytic hypotension or for improving ultrafiltration



Human albumin for intradialytic hypotension in haemodialysis patients (Review)

Fortin PM, Bassett K, Musini VM

- 1 single (N = 45) randomized crossover trial of 5% albumin compared with normal saline
- **No difference** in the primary outcome (percentage target ultrafiltration achieved) or other clinical outcomes.
- There were no significant differences in the nursing time required to treat IDH and the time to restore BP

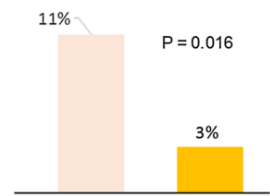


A randomized trial of albumin infusion to prevent intradialytic hypotension in hospitalized hypoalbuminemic patients

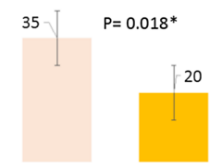
Etienne Macedo^{1*}, Bethany Karl¹, Euyhyun Lee² and Ravindra L. Mehta¹

- 2021 RCT comparing patients receiving 0.9% saline or 25% albumin at the initiation of dialysis
- 65 hospitalized patients requiring hemodialysis with serum albumin levels of < 30 g/L
- **Improvement in hypotension**, lowest intradialytic systolic BP, and ultrafiltration rate

Hypotension Episodes based on Fall20Nadir90



Total time with UF discontinued during session (min)





Cirrhosis
N=5

**Critical
Care**
N=3

**Pediatric &
Neonatal**
N=3

**CV
Surgery**
N=2

Renal
N=1

Takeaway 1

Group	Population	Indication	Stance	Strength	Evidence
Cirrhosis	Patients with cirrhosis and spontaneous bacterial peritonitis Recommended dose: Alb 20-25%, Day 1: 1.5 g/kg, Day 3: 1.0 g/kg*	Reduce mortality	For	Conditional	Low
Cirrhosis	Patients with cirrhosis and ascites undergoing large volume paracentesis (>5 liters) Recommended dose: Albumin 20-25%, 6-8 g/L of fluid removed	Prevent paracentesis-induced circulatory dysfunction	For	Conditional	Very low
Cirrhosis	Outpatients with cirrhosis and uncomplicated ascites despite diuretic therapy	Reduce complications associated with cirrhosis	Against	Conditional	Low
Cirrhosis	Hospitalized patients with decompensated cirrhosis with hypoalbuminemia (<30 g/L)	Reduce infection, kidney dysfunction or death	Against	Conditional	Low
Cirrhosis	Patients with cirrhosis and extraperitoneal infections	Reduce mortality or kidney failure	Against	Conditional	Low
CV Surg	Adult patients undergoing cardiovascular surgery	Priming the cardiovascular bypass circuit or volume replacement	Against	Conditional	Moderate
CV Surg	Pediatric patients undergoing cardiovascular surgery	Priming the cardiovascular bypass circuit or volume replacement	Against	Conditional	Very low
ICU	Critically ill adults (excluding thermal injuries and ARDS)	First-line volume replacement or increase serum albumin levels	Against	Conditional	Moderate
ICU	Critically ill adults	Removal of extravascular fluid with diuretics	Against	Conditional	Very low
ICU	Critically ill adults with thermal injuries or ARDS	Volume replacement or increase serum albumin level	Against	Conditional	Very low
Neonate	Preterm neonates (<36 weeks) with low serum albumin levels and respiratory distress	Improve respiratory function	Against	Conditional	Very low
Neonate	Preterm neonates (<32 weeks or <1,500 g) with or without hypoperfusion	Volume replacement	Against	Conditional	Very low
Peds	Pediatric patients with infection and hypoperfusion	Reduce mortality	Against	Strong	Low
Renal	Patients undergoing renal replacement therapy	Prevention or treatment of intradialytic hypotension or improving ultrafiltration	Against	Conditional	Very low

Takeaway 2



Takeaway 3



Ongoing implementation research project

Objective:

- Using a behavioural science approach to support the implementation of recommendations in ICTMG's clinical guideline on albumin use.

Next steps:

- Survey healthcare providers in Canada about barriers and enablers to using specific recommendations in the new ICTMG albumin clinical guideline.

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Interested in supporting and participating in such projects?

Reach out info@ictmg.org

Thank you

Kimberly Figures
Abby Wolfe
Casey Kapitany



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Questions

