Preferences for albumin use in adult intensive care unit patients with shock

An international survey

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RESEARCH ARTICLE

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Preferences for albumin use in adult intensive care unit patients with shock: An international survey

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Abstract

Introduction: Use of albumin is suggested for some patients with shock, but preferences for its use may vary among intensive care unit (ICU) physicians.

Methods: We conducted an international online survey of ICU physicians with 20 questions about their use of albumin and their opinion towards a randomised trial among adults with shock comparing the use versus no use of albumin.

Results: A total of 1248 respondents participated, with a mean response rate of 37%, ranging from 18% to 75% across 21 countries. Respondents mainly worked in mixed ICUs and 92% were specialists in intensive care medicine. The reported use of albumin in general shock varied as 18% reported 'almost never', 22% 'rarely', 34% 'occasionally', 22% 'frequently' and 4% 'almost always' using albumin. In septic shock, 19% reported 'almost never', 22% 'rarely', 29% 'occasionally', 22% 'frequently' and 7% 'almost always' using albumin. Physicians' preferences were more consistent for haemorrhagic- and cardiogenic shock, with more than 45% reporting 'almost never' using albumin. While the reported use of albumin for other purposes than resuscitation was infrequent (40%–85% reported 'almost never' for five other indications), the most frequent other indications were low serum albumin levels and improvement of the efficacy of diuretics. Most respondents (93%) would randomise adult ICU patients with shock to a trial of albumin versus no albumin.

For affiliations refer to page 1241

Conclusions: In this international survey, the reported preferences for the use of albumin in adult ICU patients with shock varied considerably among surveyed ICU physicians. The support for a future randomised trial was high.

KEYWORDS
albumin, fluid therapy, intensive care unit, shock, survey

Editorial Comment

This international survey of the opinions of critical care physicians shows variability in the opinions of the use of albumin in patients with shock. The majority of physician supports further trials on albumin as a resuscitation fluid.

1 | INTRODUCTION

Albumin's role as a resuscitative fluid in the critical care setting is the subject of ongoing debate.[1–3] Albumin is more likely to maintain oncotic pressure than crystalloids, which in theory may have volume-sparing effects.[4–6] Additionally, albumin may be used to correct hypoalbuminemia, which often accompanies critical illness and has been associated with poor clinical outcomes.[7] Despite this, no firm evidence has shown superiority of albumin solutions as compared with crystalloid solutions on patient-important outcomes.[8,9]

The most recent Cochrane systematic review with meta-analysis, including 20 trials with 13,047 critically ill patients found little to no differences in 30-day or 90-day mortality with the use of albumin or fresh-frozen plasma versus crystalloids (moderate certainty of evidence).[10] However, the 2021 Surviving Sepsis Campaign guideline recommends the use of albumin in patients with sepsis or septic shock who have received large volumes of crystalloids.[11] This is a conditional recommendation based on moderate certainty evidence, largely informed by evidence of a positive effect on hemodynamic endpoints.[8,12] In 2024, the International Collaboration for Transfusion Medicine Guidelines suggested (conditional recommendation) not to use intravenous albumin for first-line volume replacement or to increase serum albumin levels in critically ill adult patients (excluding those with thermal injuries and acute respiratory distress syndrome) based on moderate certainty of evidence.[13]

Nonetheless, albumin is frequently used in daily clinical practice in the intensive care unit (ICU).[14] In a post hoc study of the Conservative versus Liberal Approach to Fluid Therapy of Septic Shock in Intensive Care (CLASSIC) trial, a European randomised clinical trial (RCT) of fluid volumes in septic shock, intravenous fluid therapy during ICU stay included albumin infusion in about half of the participants in the standard-fluid group.[15] There was substantial variation across participating ICUs that could not be explained by differences in participants' characteristics.[15]

In this international survey, we assessed ICU physicians' preferences towards using albumin in adult ICU patients with shock. In addition, we surveyed the willingness to take part in an RCT assessing use versus no use of albumin in ICU patients with shock. We hypothesised that preferences for the use of albumin would vary, supporting clinical equipoise.

2 | METHODS

2.1 | Study design, data collection and approvals

We conducted an international online survey using the secure web application Research Electronic Data Capture (REDCap) hosted by the Capital Region of Denmark.[16] The survey was pilot-tested and revised by five ICU physicians and seven researchers working at the coordinating site at Rigshospitalet, Denmark, before data collection. The survey was distributed and responses collected from December 8, 2023 to January 31, 2024. Participation in the survey was voluntary and no financial compensation was provided. Activation and completion of the survey link was considered informed consent. Respondents were encouraged to register their work e-mail address by the end of the survey. These were solely used to minimise missing data and verify the uniqueness of responses before calculating the response rate. In case of duplicate responses by the same work e-mail, we used the complete form if only one of the forms were complete; if all forms were incomplete, we contacted the respondent and requested response to missing questions; if all forms were complete, we contacted the respondent to inquire about their preference. This manuscript has been prepared and reported according to the Consensus-Based Checklist for Reporting of Survey Studies (CROSS) checklist (Supplementary Appendix 1).[17]

We obtained approval from the Legal Department of Scientific Research in the Capital Region of Denmark (approval number: p-2023-14742). Ethical approval and other approvals were waived because no patient data were collected and the only identifiable data collected from participating ICU physicians were work e-mail addresses.

2.2 | Survey description

The survey consisted of 20 main questions. The first five questions assessed respondents' characteristics including their professional setting. The following nine questions covered respondents' preferred clinical use of albumin in adult ICU patients with various types of shock and explored the use of albumin for indications other than resuscitation. For all questions was specified that the choice of

albumin concentration (4%, 5% or 20% solutions) along with the dosage and timing of administrations would be at their own discretion. Finally, the survey contained six questions assessing preferences for a future RCT comparing the use versus no use of albumin in adult ICU patients with shock. These questions assessed potential exclusion of certain patient populations with specific secondary diagnoses. We included branching logic functions and free-text fields in the survey, allowing respondents to detail potential barriers against randomising adult ICU patients with shock to either the use or no use of albumin. The distributed survey is available in Supplementary Appendix 2.

2.3 | Survey distribution

The survey was distributed as broadly as possible within an established international network for ICU research, the Collaboration for Research in Intensive Care (CRIC, www.cric.nu). Additional countries were invited based on prior survey collaboration with the CRIC network. All types of ICUs were invited to participate.

Each country had a national investigator who personally invited ICUs to participate. In each country, the national investigator or a designated local site investigator coordinated the distribution of an e-mail containing an online survey link to all physicians working in their ICU. All coordinators received a minimum of two reminders before database closure. Each national investigator reported the total number of physicians who had received the survey invitation in their respective country.

2.4 | Statistical analyses

We present data descriptively and report numbers and percentages for categorical variables and medians with interquartile ranges (IQRs) for continuous variables. The proportion of missing data are reported with no imputation of missing data. All statistical analyses were performed using R (version 4.3.2). No sample size estimation was conducted, but we distributed the survey widely with the aim of including participants from as many countries and sites as possible within an approximate two-month period. Our intention was to ensure a sample size large enough to describe trends or variations in responses.

3 | RESULTS

A total of 1248 respondents from 21 countries participated in the survey (Table 1 and Supplementary Appendix 3). Respondents mainly worked in mixed ICUs in public hospitals staffing a median of 12 beds (IQR 9–21) (Table 1). Most respondents (92%, 95% confidence interval [CI] 90%–93%) were specialists in intensive care medicine. The mean response rate was 37%, with response rates per country ranging from 18% to 75% (Table 2). Less than 2% of responses were missing for the 20 main questions in the survey (Supplementary Appendix 4).

TABLE 1 Characteristics of respondents.

	N	Percentages (95% CI)
Specialist	1142	91.5% (89.8–93.1%)
Country[a]		
Denmark	279	22.4% (20.1–24.7%)
Norway	175	14.1% (12.1–16.0%)
The United Kingdom	112	9.0% (7.5–10.6%)
Sweden	105	8.4% (6.9–10.0%)
Finland	72	5.8% (4.5–7.1%)
Switzerland	63	5.1% (3.9–6.3%)
Belgium	58	4.7% (3.5–5.9%)
The Czech Republic	47	3.8% (2.7–4.9%)
Lithuania	43	3.5% (2.5–4.5%)
Italy	33	2.7% (1.8–3.6%)
Estonia	33	2.7% (1.8–3.6%)
Turkey	30	2.4% (1.6–3.3%)
Kuwait	26	2.1% (1.4–2.9%)
Poland	24	1.9% (1.2–2.7%)
Japan	23	1.8% (1.1–2.7%)
New Zealand	23	1.8% (1.1–2.7%)
The Netherlands	22	1.8% (1.0–2.6%)
The United Arab Emirates	21	1.7% (1.0–2.4%)
The United States	20	1.6% (1.0–2.3%)
Iceland	18	1.4% (0.8–2.2%)
Saudi Arabia	18	1.4% (0.8–2.2%)
Type of hospital		
Public specialist hospital	613	49.1% (46.3–51.9%)
Public general hospital	583	46.7% (43.9–49.5%)
Private specialist hospital	29	2.3% (1.5–3.2%)
Private general hospital	23	1.8% (1.1–2.6%)
Type of ICU		
Mixed ICU	1037	83.1% (81.0–85.2%)
Cardiothoracic ICU	66	5.3% (4.1–6.6%)
Medical ICU	59	4.7% (3.6–5.9%)
Neurological/neurosurgical ICU	43	3.4% (2.5–4.5%)
Surgical ICU	43	3.4% (2.5–4.5%)
Number of beds per ICU[b]	12.0	(9.0–21.0)

Note: All respondents ($n = 1248$). Counts with percentages and 95% confidence interval (CI) or median with IQR.
[a]Fourteen participants had not stated number of beds in their ICU.
[b]Three participants had not reported country.

3.1 | Preferences for the use of albumin in shock

In adult ICU patients with shock, 18% (95% CI 16%–20%) reported 'almost never', 22% (95% CI 20%–25%) 'rarely', 34% (95% CI 31%–37%) 'occasionally', 22% (95% CI 19%–24%) 'frequently' and 4% (95% CI 3%–5%) 'almost always' using albumin (Figure 1 and Supplementary Appendix 5). When considering types of shock, a similar

TABLE 2 Number of respondents per country.

Country	Number of respondents/ number invited physicians (response rate)
Denmark	279/610 (46%)
Norway	175/650 (27%)
The United Kingdom	112/282 (40%)
Sweden	105/175 (60%)
Finland	72/198 (36%)
Switzerland	63/213 (30%)
Belgium	58/318 (18%)
The Czech Republic	47/115 (41%)
Lithuania	43/113 (38%)
Estonia	33/77 (43%)
Italy	33/140 (24%)
Turkey	30/52 (58%)
Kuwait	26/50 (52%)
New Zealand	24/46 (52%)
Poland	24/32 (75%)
The Netherlands	23/46 (50%)
The United Arab Emirates	22/117 (19%)
The United States	21/30 (70%)
Iceland	20/48 (42%)
Japan	18/28 (64%)
Saudi Arabia	18/25 (72%)

pattern was seen for patients with septic shock, with the exception that more seemed to report 'almost always' using albumin. For septic shock 19% (95% CI 17%–21%) reported 'almost never', 22% (95% CI 20%–25%) 'rarely', 29% (95% CI 27%–32%) 'occasionally', 22% (95% CI 20%–25%) 'frequently' and 7% (95% CI 6%–9%) 'almost always' using albumin (Supplementary Appendix 6). However, in haemorrhagic and cardiogenic shock, more than 45% of respondents reported 'almost never' using albumin (Figure 1 and Supplementary Appendix 7 and 8).

Most respondents indicated 'almost never' using albumin for purposes other than for resuscitation in ICU patients with shock, ranging between 40% and 45% when addressing low albumin levels or enhancing efficacy of diuretics (Figure 2 and Supplementary Appendix 9–13). The range for 'almost never' fell between 70% and 85% for purposes such as improving the immune function, drug-carrying capacity, or correcting acid base-disturbances. Preferences for serum albumin levels to substitute albumin in adult ICU patients with shock without evident albumin loss are detailed in Table 2.

3.2 | Preferences for a future randomised trial

Most of the respondents (93%) supported a future RCT investigating the use versus no use of albumin for resuscitation of adult ICU patients with shock. In a future RCT, correction of low serum albumin levels in adult ICU patients with shock was generally considered a valid indication for using albumin (Table 3).

In a future RCT, the respondents indicated their intention to exclude certain patient populations with specific secondary diagnoses (Table 3). Among these, traumatic brain injury had the highest rating at 32% (95% CI 28%–37%), while other secondary diagnoses ranged from 6% to 20%. However, nearly 39% (95% CI 34%–43%) of respondents would include all patients regardless of the mentioned secondary diagnoses.

In the scenario of a future, adequately powered, high-quality RCT showing similar results on patient-important outcomes, 63% (95% CI 60%–66%) indicated physiological or surrogate outcomes as influential factors in their decision to use albumin. This was followed by 41% (95% CI 36%–45%) considering price, 26% (95% CI 21%–31%) availability and 21% (95% CI 16%–26%) the climate impact. However, 20% (95% CI 15%–25%) appeared unaffected by these factors.

4 | DISCUSSION

In this international survey, we found that the reported use of albumin in ICU patients with shock varied among surveyed ICU physicians. The greatest variation was observed for septic shock, whereas the reported use in haemorrhagic- and cardiogenic shock was more consistent, with almost half of the respondents indicating almost never using albumin. The use of albumin for other indications than resuscitation was infrequent. More than 9 out of 10 respondents supported a future RCT investigating the use versus no use of albumin in adult ICU patients with shock.

Our findings complement the results of a previous survey among 1097 critical care- and emergency department physicians across Canada, the United Kingdom, Scandinavia and Saudi Arabia in 2016, which investigated resuscitation practices in adult patients with early septic shock.[18] Herein, 71% of critical care physicians indicated 'never/rarely' administering 5% albumin, while 81% reported 'never/rarely' administering 20% or 25% albumin. In our survey, only 19% reported 'almost never' and 22% indicated 'rarely' using albumin in patients with septic shock, which may indicate a more frequent self-reported use in our survey. Yet, consistent with our findings, 88% of respondents supported investigation of albumin in a trial setting.[18]

Currently, the best available evidence for the use of albumin is in patients with cirrhosis, particularly for treatment after large-volume paracentesis,[19–21] in the treatment of hepatorenal syndrome,[20] and as part of treatment for spontaneous bacterial peritonitis.[22] Meanwhile, albumin use outside of these specific conditions including shock remains controversial.[3]

In the most recent Cochrane review assessing albumin or fresh-frozen plasma versus crystalloids in critically ill patients, only four trials included patients with shock (hypovolemic, septic, burn, or combined septic and hypovolemic shock).[10] The trials tested various indications for albumin such as resuscitation and correction or maintenance of serum albumin levels. In a mixed ICU population, the largest RCT comparing 4% albumin versus saline for fluid resuscitation in

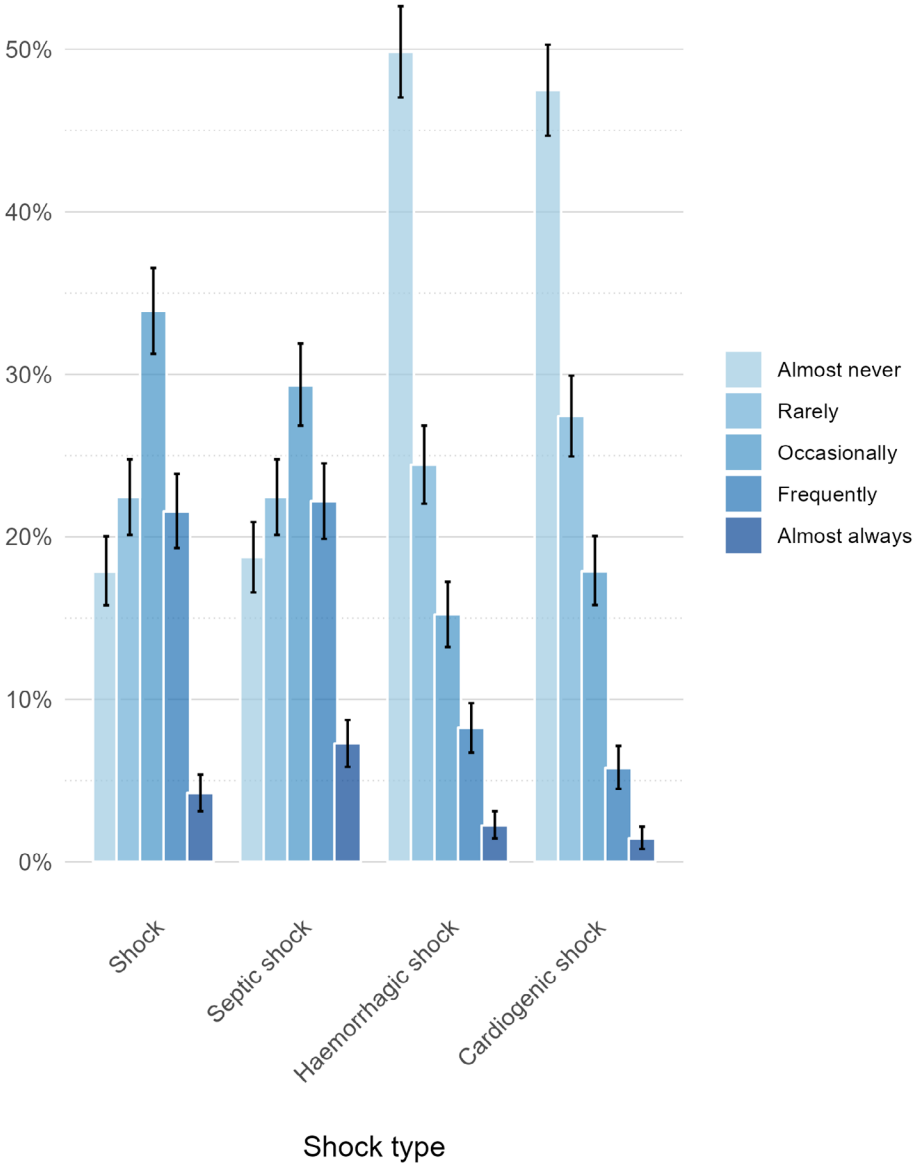

FIGURE 1 Albumin use in shock: Bar plots illustrating the percentage of survey respondents' reported use of albumin in intensive care unit patients with shock, categorised by overall use in shock and the specific shock types (septic shock, haemorrhagic shock and cardiogenic shock). The black bars represent 95% confidence intervals for each category. One participant had not responded preference regarding cardiogenic shock.

6997 adult ICU patients (SAFE trial) found similar effects on patient-important outcomes.[9] Subsequently, a post hoc analysis including 1218 patients with severe sepsis indicated that resuscitation with 4% albumin as compared to saline might reduce mortality.[23] However, a later RCT assessing replacement with 20% albumin in addition to crystalloids as compared to crystalloid solution alone in 1818 ICU patients with severe sepsis or septic shock (ALBIOS trial) found similar mortality rates.[8]

Contrastingly, there are specific subpopulations such as patients with traumatic brain injury, where the use of albumin may be harmful.[24] Somewhat surprisingly, 39% of respondents in our survey would not exclude any patients with specific secondary diagnoses in a future RCT assessing the use versus no use of albumin in shock, whereas only 32% indicated exclusion of patients with traumatic brain injury.

Hypoalbuminemia is common among critically ill patients and is associated with poor outcomes.[7] A meta-analysis evaluating hypoalbuminemia as a prognostic marker across 90 studies including critically ill patients found that hypoalbuminemia was associated with increased mortality, morbidity and length of hospital stay.[7] Yet, the question remains if albumin replacement improves outcomes or if hypoalbuminemia is just a marker for severity of illness, supporting recent guidelines, in which the replacement of albumin was not recommended.[13]

Albumin has been suggested to be beneficial for other indications such as potentiation of drugs due to its drug binding and transporting capacity,[2] positive impact on the immune function based on the antioxidant effect of albumin,[25] and a potential impact on acid base disturbances.[26] However, these findings have mainly been observed in pre-clinical studies or in studies of specific populations, which limits their applicability in a heterogenous population of adult ICU patients.[26] This is likely reflected in the results of our survey in which only few respondents considered the use of albumin for secondary purposes other than resuscitation.

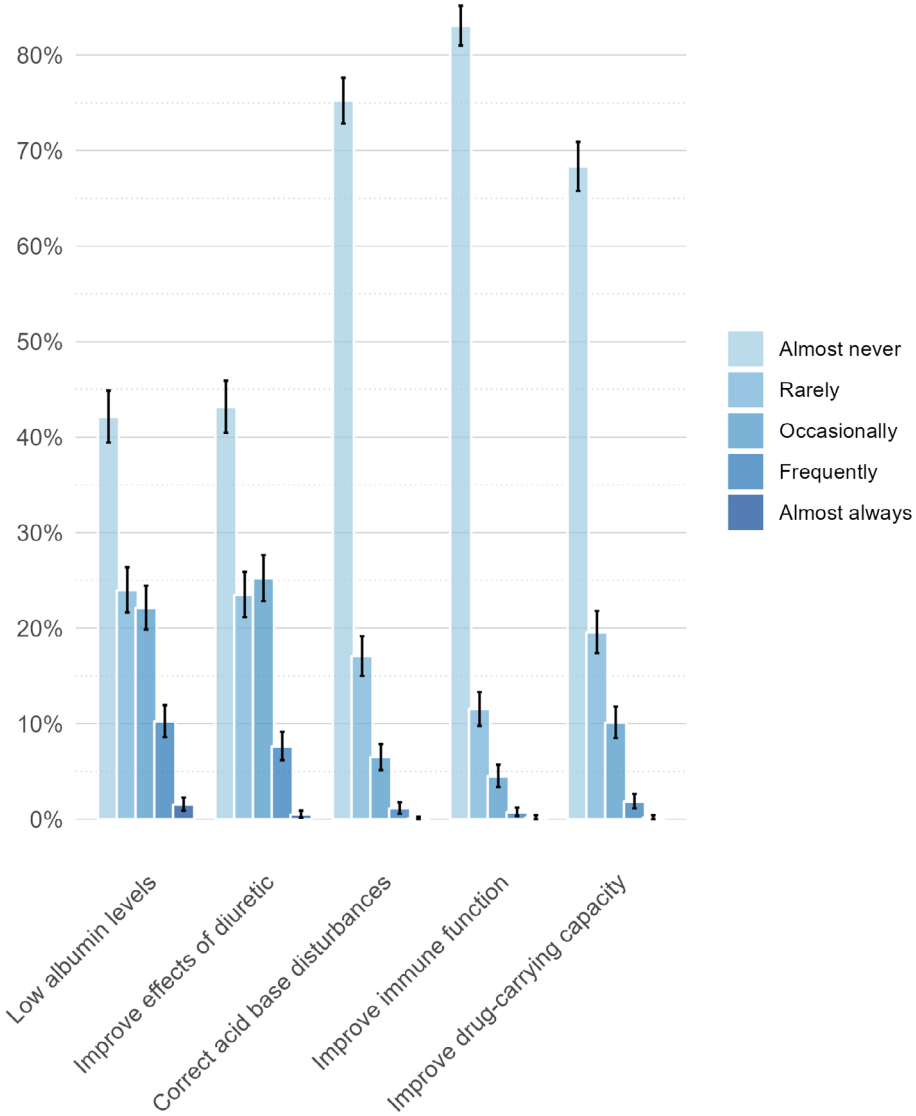

FIGURE 2 Albumin use in shock for purposes other than resuscitation: Bar plots illustrating the percentage of reported use of albumin in intensive care unit patients with shock for purposes other than for resuscitation that is, low serum albumin levels, improve effects of diuretics, improve the immune function, correct acid/base-disturbances and improve the drug-carrying capacity. The black bars represent 95% confidence intervals for each category.

Taken together, the variation in self-reported practice likely reflects a limited evidence base. Moreover, the support for a future RCT was high among surveyed ICU physicians. The responses from this survey will inform the planning of such a RCT.

4.1 | Strengths and limitations

The strength of this survey includes its international scope, resulting in reasonable external validity. More than 90% of the respondents were specialists in intensive care medicine. In addition, we had limited missing data with less than 2% of main questions left unanswered. There are also limitations. First, the overall response rate was 37%, which limits the generalisability as those who responded may have a stronger interest in the topic and their responses may differ from that of non-responders. Second, the proportion of respondents per country varied considerably, as invitations were at the discretion of national investigators, potentially introducing selection bias. Third, there is an inherent possibility of response bias, as respondents could consciously or unconsciously provide answers they perceive as more favourable or aligned with expectations. Fourth, only 10% of respondents resided in non-European countries, hence limiting the external validity outside of Europe and precluding comparisons of responses from different geographic regions. Fifth, as the applied secure web application, REDCap, allowed for submission of uncompleted forms some data were missing. We sought to limit this by contacting respondents with incomplete forms if e-mail addresses were provided. However, we included all responses, regardless of completeness, in our analysis. Finally, almost 18% of responders did not include e-mail addresses, also raising the possibility of duplicate entries within this subset.

5 | CONCLUSIONS

In this international survey, the reported preferences for the use of albumin in adult ICU patients with shock varied considerably among surveyed ICU physicians. Most respondents (93%) supported a future

TABLE 3 Preference for substitution and future trial considerations.

Preferred levels for substitution of albumin	N	Percentages (95% CI)
How often do you use albumin to correct low serum levels in adult patients with shock and no apparent loss of albumin?	$n = 1248$	
Almost never	526 (42%)	42% (39–45%)
Rarely	299 (24%)	24% (22–26%)
Occasionally	276 (22%)	22% (20–24%)
Frequently	128 (10%)	10% (9–12%)
Almost always	19 (2%)	2% (1–2%)
At what serum albumin level would you administer albumin?	$n = 722$[a]	
S-albumin <15 g/L	140	19% (16–22%)
S-albumin <20 g/L	338	47% (43–50%)
S-albumin <25 g/L	172	24% (21–27%)
S-albumin <30 g/L	54	7% (6–9%)
S-albumin <35 g/L	7	1% (0–2%)
Other (range 0–99 g/L)[b]	11	
Preferences for the use of albumin in a future randomised trial		
Would you accept to randomise patients to routinely use albumin in addition to crystalloids during circulatory failure?	$n = 1248$	
Yes	1159	93%c (92–94%)
Would you accept to randomise patients to routinely avoid the use of albumin during circulatory failure?		
Yes	1165	93% (92–95%)
Would you accept to randomise patients to routinely use albumin to correct low serum albumin level?		
Yes	1046	84%[d] (82–86%)
In a future trial, at what serum albumin level would you prefer to correct low serum albumin levels?		
S-albumin <15 g/L	220 (21%)	21% (19–24%)
S-albumin <20 g/L	487 (47%)	47% (44–50%)
S-albumin <25 g/L	248 (24%)	24% (21–26%)
S-albumin <30 g/L	69 (7%)	7% (5–8%)
S-albumin <35 g/L	10 (1%)	1% (0–2%)
Other (range 0 to 99 g/L)[e]	10 (1%)	
Would you accept to randomise patients to routinely avoid the use of albumin in cases of low serum albumin levels?		
Yes	1092	88%d (86–89%)
In a future trial, below which serum albumin level would you refuse to avoid albumin?		
S-albumin <15 g/L	493 (45%)	45% (42–48%)
S-albumin <20 g/L	239 (22%)	22% (20–24%)
S-albumin <25 g/L	108 (10%)	10% (8–12%)
S-albumin <30 g/L	66 (6%)	6% (5–8%)
S-albumin <35 g/L	46 (4%)	4% (3–5%)
Other (range 0–18 g/L)[f]	135 (12%)	

TABLE 3 (Continued)

Preferred levels for substitution of albumin	N	Percentages (95% CI)
Would you REFUSE to enrol patients with shock in a trial comparing the use of albumin versus no albumin if patients had any of the following secondary diagnoses?[g]		
Traumatic brain injury	401	32% (28–37%)
Haemorrhagic shock and uncontrolled bleeding	256	21% (16–25%)
Burns >10% of the body surface area	238	19% (14–24%)
Chronic liver disease (any stage)	230	18% (13–23%)
Severe congestive heart failure (NYHA III and IV classes)	223	18% (13–23%)
Meningitis or other neuro-infection	187	15% (10–20%)
Post liver transplantation	185	15% (10–20%)
Stroke	130	10% (5–16%)
Acute respiratory distress syndrome	119	10% (5–15%)
Haemorrhagic shock and controlled bleeding	117	9% (4–15%)
Trauma	103	8% (3–14%)
Solid organ transplantation other than liver transplantation	71	6% (1–11%)

[a]Totally 722 respondents correspond to number of respondents who would substitute albumin 'rarely', 'occasionally', 'frequently' or 'almost always' in question.
[b]Four (0.6%, 95% CI 0.1–1.1%) suggested 10 g/L, three (0.4%, 95% CI 0.0–1.0%) other respondents suggested 0 g/L and single (0.1%, 95% CI 0.0–0.4%) respondents suggested 5, 12, 18 and 99 g/L, respectively.
[c]2 respondents with missing responses.
[d]1 participant with missing response.
[e]3 respondents suggested 0 g/L, 3 other respondents suggested 10 g/L and single respondents suggested 12, 17, 18 and 99 g/L, respectively.
[f]59 (5%, 95% CI 4–7%) respondents suggested 10 g/L, 51 (5%, 95% CI 3–6%) respondents suggested 0 g/L, nine (0.8%, 95% CI 0.4–1.4%) respondents suggested 12 g/L, seven (0.6%, 95% CI 0.2–1.2%) respondents suggested 5 g/L, four (0.4%, 95% CI 0.1–0.7%) respondents suggested 1 g/L, while single (0.1%, 95% CI 0.0–0.3%) respondents suggested 8, 11,13, 18 and 99 g/L, respectively.
[g]482 (39%) accepted to randomise regardless of the diagnoses mentioned.

RCT in adult ICU patients with shock comparing the use versus no use of albumin.

AUTHOR CONTRBUTIONS

Cepceptualisation and study design: PS, AP, MHM, AG and TM. Data analysis: PS. Writing first draft: PS, KE and TM. Critical review and approval of manuscript: all authors.

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CONFLICT OF INTEREST STATEMENT

PS, KLE, AP, MHM, AG and TM are involved in the design of a domain on the Intensive Care Platform Trial (INCEPT, www.incept.dk) investigating the use of albumin. INCEPT is funded by Sygeforsikringen 'danmark' and the Novo Nordisk Foundation and supported by Grosserer Jakob Ehrenreich and Hustru Grete Ehrenreich Foundation, Dagmar Marshalls Foundation and Savværksejer Jeppe Juhl and Ovita Juhls Mindelegat. PS, KLE, AP, MHM, AG and TM are affiliated with the Department of Intensive Care at Rigshospitalet, which has received funding for other projects from the Novo Nordisk Foundation. PS received funding from the Research Council of Rigshospitalet and Jakob Ehrenreich and his wife Grete Ehrenreich's Foundation. AP has received an honorarium from Novartis for participation in an advisory board. JDW has consulted for Menarini, MSD, Pfizer, ThermoFisher and Viatris with fees and honoraria paid to institution. JH has received an honorarium from Paion for participation in an advisory board. ARB received speaker or consultancy fees from Nutricia Danone and VIPUN Medical and she is holding a grant from the Estonian Research Council. AK currently consults for or has consulted for Medtronic, Edwards Life Sciences, Philips Research North America, Baxter, GE Healthcare, Potrero Medical, Fifth Eye Inc., Retia Medical, Caretaker Medical, Renibus Therapeutics, Trevena Pharmaceuticals and Pharmazz Inc. AK is also a member of the Surviving Sepsis Guidelines Research Committee, SCCM ESICM joint task force on Norepinephrine formulations and Chairs the SCCMM Discovery Research Network. The remaining authors declare no conflicts of interest. The funders had no influence on the design, conduct or the decision to publish the results of this manuscript.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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