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Low Serum Albumin as a Determinant of Mortality in Shock: A Systematic Review and Meta-Analysis of Global Evidence

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Abstract

Background: Hypoalbuminemia is a hallmark of critical illness, reflecting both systemic inflammation and impaired homeostasis. This systematic review and meta-analysis examine the prognostic significance of low serum albumin in shock patients, integrating data from diverse global cohorts. Methods: Comprehensive searches of PubMed, Europe PMC, and Google Scholar were conducted (2019-2025) to identify studies reporting adjusted odds ratios (ORs) or hazard ratios (HRs) for the association between hypoalbuminemia and mortality in adult shock patients. Separate random-effects meta-analyses were performed for ORs and HRs. Heterogeneity was quantified with I^2 statistics, and meta-regression was applied to explore study-level covariates. Results: Eleven studies met inclusion criteria (n = 7 OR studies; n = 4 HR studies). Pooled ORs and HRs each demonstrated a robust association between low serum albumin and increased mortality, independent of major confounders. Sensitivity analyses confirmed the stability of findings. Age significantly modified OR-based associations, while continental location showed borderline influence in HR models. Conclusions: Low serum albumin is a powerful, independent prognostic biomarker in shock. These findings reinforce albumin's potential utility

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in risk stratification and therapeutic decision-making in critical care.

Keywords

Hypoalbuminemia, Shock, Mortality

1. Introduction

Shock, a fulminant syndrome of circulatory collapse and tissue hypoperfusion, remains one of the most formidable challenges in critical care [1]-[3]. Despite advances in hemodynamic monitoring, organ support, and targeted therapies, mortality rates remain unacceptably high [4]-[10]. The quest for reliable biomarkers that can anticipate outcomes, guide interventions, and refine prognostic accuracy is both urgent and ongoing [11]-[17].

Albumin, the most abundant plasma protein, is traditionally recognized for its role in oncotic pressure maintenance [18]-[23]. However, its clinical significance extends far beyond simple fluid balance. Albumin functions as a transporter, antioxidant, and modulator of inflammation [24]-[29].

Hypoalbuminemia—whether due to capillary leak, hepatic synthetic failure, or catabolic degradation—is not merely an epiphenomenon but may contribute causally to organ dysfunction and adverse outcomes [30]-[34].

Although individual studies have linked low serum albumin to increased mortality in shock, the magnitude, consistency, and potential modifiers of this association have not been comprehensively quantified. The present systematic review and meta-analysis aims to fill this knowledge gap, leveraging global data to clarify the prognostic role of hypoalbuminemia in shock.

2. Methods

This systematic review and meta-analysis adhered to PRISMA 2020 guidelines [35]-[40] and was prospectively registered with PROSPERO under the ID number: CD420251132055 (https://www.crd.york.ac.uk/PROSPERO/view/CRD420251132055) [41] [42]. Two independent reviewers oversaw each phase of the review—screening, eligibility assessment, study selection, and inclusion—resolving disagreements through consultation with a third reviewer.

2.1. Search Strategy

We systematically searched PubMed, Europe PMC, and Google Scholar from January 1, 2019, to January 31, 2025, using controlled vocabulary and keyword combinations encompassing “hypoalbuminemia”, “serum albumin”, “shock”, “mortality”, and “prognosis”. The full search strategy is detailed in **Table 1**. Grey literature sources were screened, and corresponding authors of eligible studies were contacted to obtain missing data.

Table 1. Search query used at different search engine.

DATABASE	Search Terms
PubMed	((((((hypoalbuminemia[MeSH Terms]) OR (albumin[MeSH Terms])) AND (shock[Title/Abstract])) AND (mortality[Title/Abstract])) OR (prognosis[Title/Abstract])) AND (("2019/01/01"[Date - Publication]: "2025/01/31"[Date - Publication]))) AND (english[Language])
Europe PMC	((((TITLE_ABS:(hypoalbuminemia) OR TITLE_ABS:(serum albumin)) AND TITLE_ABS:(shock)) AND TITLE_ABS:(mortality)) OR TITLE_ABS:(prognosis)) AND (FIRST_PDATE: [2019 TO 2025])
Google Scholar	((hypoalbuminemia) OR (serum albumin)) AND (shock) AND ((mortality) OR (prognosis)) AND (2019-2025)

2.2. Eligibility Criteria

The eligibility criteria are presented in Table 2. Inclusion criteria were observational cohort studies involving adult shock patients, serum albumin measurement at baseline, comparison between hypoalbuminemic and normoalbuminemic groups, and reporting of adjusted ORs or HRs for mortality. Studies involving infants, adolescents, non-English publications, and those without effect size reporting were excluded (Table 2).

Table 2. Eligibility.

Inclusion criteria	Exclusion criteria
Observational studies	Infants and adolescents
Patients: shock patients	Not published in English
Comparing hypoalbuminemia patients with normoalbuminemia patients	Review articles, editorials, comments.
Outcome available: odds Ratio and hazard ratio	Articles published before 2019
Serum albumin measurements available.	

Definition of Shock

For the purposes of this review, shock was defined as a clinical syndrome of acute circulatory failure characterized by tissue hypoperfusion and inadequate oxygen utilization, resulting in cellular dysfunction and organ injury. Eligible studies included patients with distributive (septic), cardiogenic, hypovolemic, or mixed shock, as defined by the original investigators. Diagnostic criteria generally encompassed hypotension (systolic blood pressure < 90 mmHg, mean arterial pressure < 65 mmHg, or requirement for vasopressor support), clinical or biochemical evidence of tissue hypoperfusion (e.g., elevated lactate), and the presence of acute organ dysfunction. Serum albumin levels were required to be measured within the first 24 - 48 hours of shock recognition or ICU admission to ensure temporal relevance to the acute episode [43].

2.3. Data Extraction and Quality Assessment

From each eligible study, we extracted publication year, geographic region, study

design, participant demographics, albumin cut-off values, effect estimates, adjustment covariates, and mortality definitions. Data extraction was conducted in duplicate using standardized forms, with discrepancies resolved by consensus. Risk of bias and Quality Assessment were evaluated using the Newcastle-Ottawa Scale (NOS), with scores ≥ 7 indicating high quality [44]-[46].

2.4. Statistical Analysis

Random-effects models (DerSimonian-Laird method) were applied to pool effect estimates, expressed as ORs or HRs with 95% confidence intervals (CIs).

Justification of the DerSimonian-Laird Estimator

A random-effects model was applied to account for expected variability across studies in populations, settings, and albumin thresholds. The DerSimonian-Laird method was chosen to estimate between-study variance (τ^2) because it remains the most widely used and cited estimator in biomedical meta-analyses. Its computational simplicity, transparency, and comparability with prior critical care and sepsis literature allow readers to benchmark our findings against existing evidence. Although alternative estimators such as restricted maximum likelihood (REML) or Paule-Mandel may provide more efficient estimates under some conditions, the DerSimonian-Laird approach ensures methodological consistency with the majority of published meta-analyses in this field, while sensitivity analyses confirmed that effect sizes were robust across estimator choice [47].

Heterogeneity was quantified with the I^2 statistic and Cochran's Q test. Meta-regression (REML estimation) was performed to assess the influence of continent, year of data collection, albumin cut-off, mean/median age, and male proportion on effect sizes. Sensitivity analyses were conducted by sequentially excluding individual studies. Analyses were performed using RevMan Web and Python-based custom scripts [48]-[53].

Hartung-Knapp Adjustment

We conducted a sensitivity analysis using the Hartung-Knapp adjustment for random-effects meta-analysis, paired with the DerSimonian-Laird between-study variance (τ^2). Relative to the conventional normal-based random-effects summary, Hartung-Knapp widens confidence intervals by using a t-distribution and an empirical variance estimator, which is particularly relevant with small numbers of studies [54].

3. Results

Search Results: The database search yielded 568,758 records, with 566,998 removed as duplicates or ineligible by automated tools. Title/abstract screening excluded 1722 of the remaining 1760 records. Thirty-eight full-text articles were assessed for eligibility, resulting in 11 studies included in the final synthesis (**Figure 1**).

In **Table 3**, risk of bias was evaluated for all 11 included cohort studies using the Newcastle-Ottawa Scale (NOS). The majority of studies (n > 10) achieved high-quality ratings (7 - 9 stars), reflecting low risk of bias. A smaller number

scored in the moderate-quality range (5 - 6 stars), typically due to limited adjustment for potential confounders in the comparability domain. All studies received full scores in the selection domain, indicating representative shock patient cohorts, appropriate non-exposed comparators, and objective ascertainment of serum albumin levels. The outcome domain was also consistently strong, with complete and objective mortality ascertainment and adequate follow-up in all cases. The primary limitation observed was that some studies adjusted only for age or a limited set of covariates, rather than a broader range of important prognostic factors, which may allow residual confounding. Overall, the methodological quality of the included studies was high, supporting the validity of the meta-analysis findings.

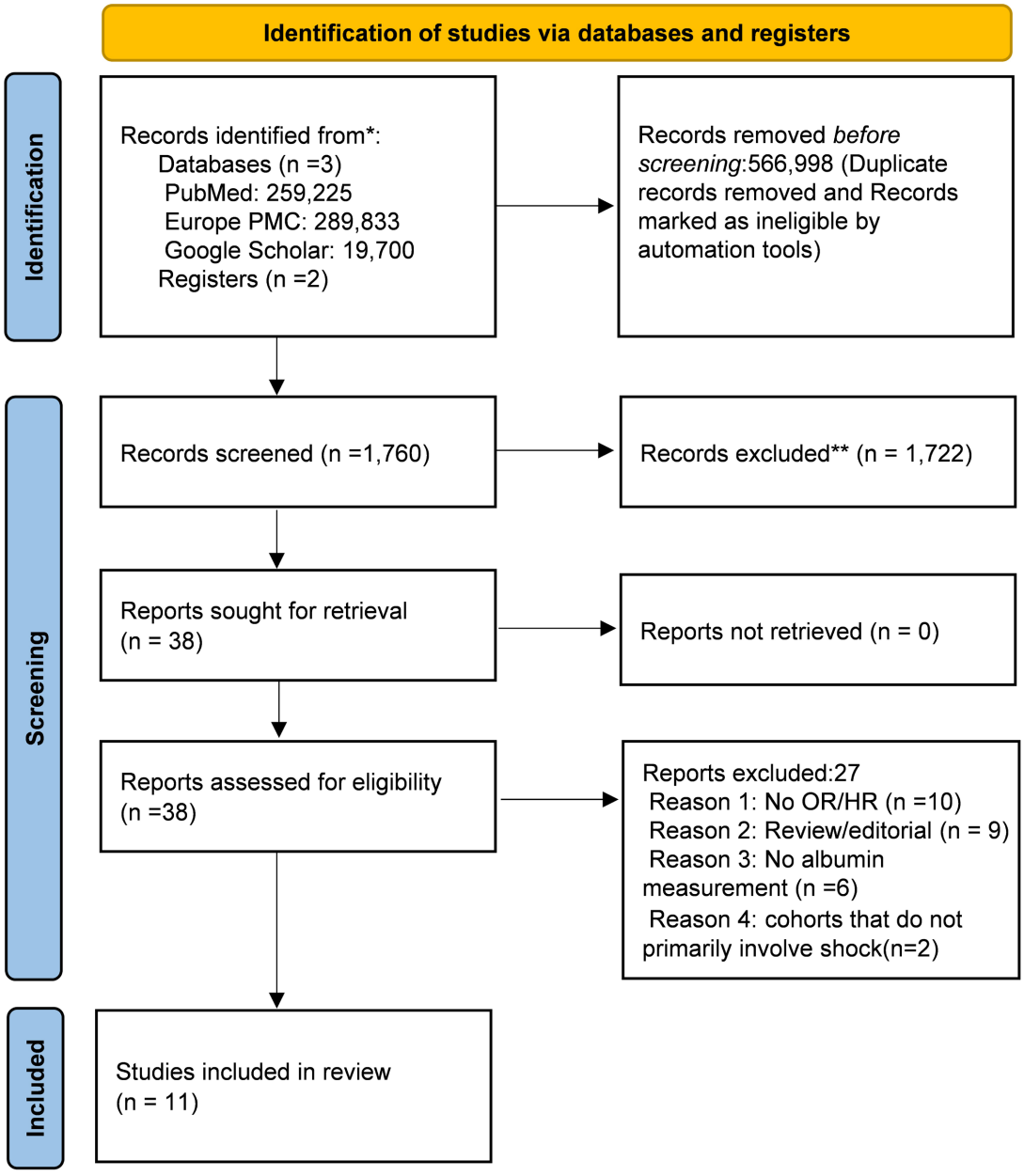


Figure 1. PRISMA flow chart for the association between hypoalbuminemia and mortality among shock patients.

Table 3. Quality and bias assessment of included studies.

Study ID	Selection: Representativeness	Selection: Non-exposed cohort	Selection: Ascertainment of exposure	Selection: Outcome not present at start	Comparability: Main factor	Comparability: Additional factors	Outcome: Assessment of outcome	Outcome: Follow-up long enough	Outcome: Adequacy of follow-up	NOS Total (0 - 9)	Overall Assessment
Mingjie Huang 2020 [55]	★	★	★	★	★		★	★	★	8	High quality (Low risk of bias)
Mitchell Padkins 2021 [56]	★	★	★	★			★	★	★	7	High quality (Low risk of bias)
Razan Rabi 2024 [57]	★	★	★	★	★	★	★	★	★	9	High quality (Low risk of bias)
Sang-Min Lee 2023 [58]	★	★	★	★			★	★	★	7	High quality (Low risk of bias)
Sha Huang 2024 [59]	★	★	★	★			★	★	★	7	High quality (Low risk of bias)
Tae Gun Shin 2019 [60]	★	★	★	★		★	★	★	★	8	High quality (Low risk of bias)
Toni Jantti 2019 [61]	★	★	★	★			★	★	★	7	High quality (Low risk of bias)
Tobias Schupp *et al.* 2023. [62]	★	★	★	★			★	★	★	7	High quality (Low risk of bias)
Song-Zan Qian 2019. [63]	★	★	★	★	★	★	★	★	★	9	High quality (Low risk of bias)
Saeid Mirzai 2024 64]	★	★	★	★	★		★	★	★	8	High quality (Low risk of bias)
Danfeng Ren 2025 [65]	★	★	★	★	★	★	★	★	★	9	High quality (Low risk of bias)

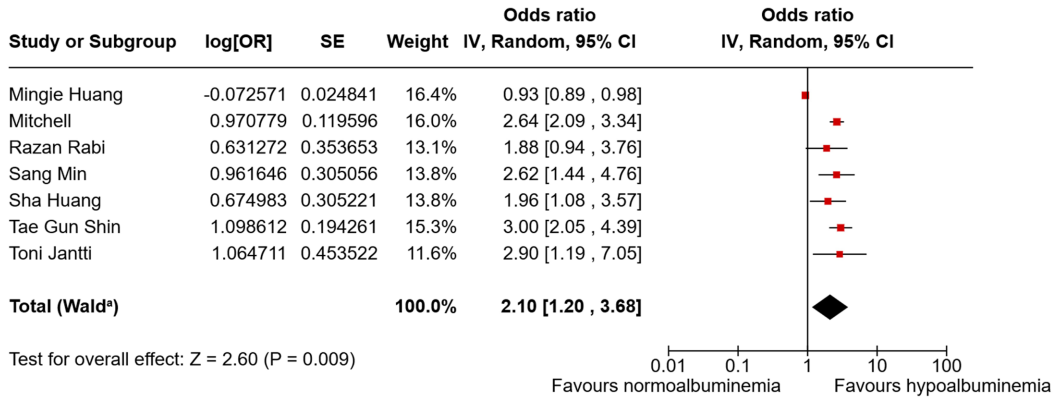
Notes: NOS scoring followed the cohort-study template. Selection items were awarded based on ICU/septic shock cohorts with laboratory-confirmed albumin exposure and mortality measured after baseline. Comparability starred once for adjustment of key confounders and additionally if age plus ≥ 1 comorbidity/clinical severity variable were adjusted. Outcome items were starred for medical-record ascertainment and sufficient follow-up (in-hospital or 30-day). Where reporting was unclear, conservative assumptions were applied.

Study Characteristics: Summary of Included Studies is presented in **Table 4**. The studies represented four continents, with Asia contributing nearly half of all included studies. Most were retrospective cohort designs (n = 11), with two prospective cohorts. Albumin cut-offs ranged from 2.45 g/dL to 40 g/L. Mortality endpoints included 30-day, in-hospital, and 1-year mortality. All studies adjusted for key clinical covariates.

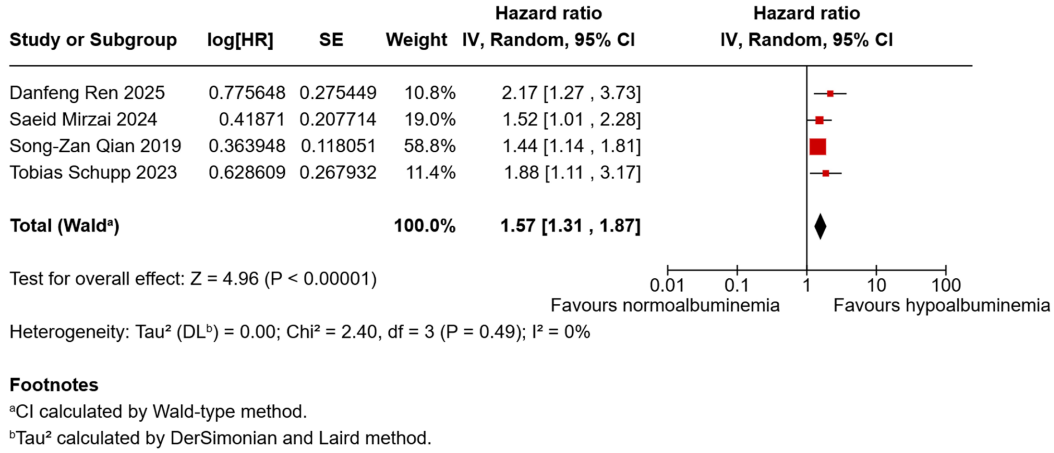
Figure 2 presents the forest plot of the meta-analysis of the association between hypoalbuminemia and mortality in shock patients. In **Figure 2(a)**, the forest plot of the seven included studies demonstrates a consistent association between hypoalbuminemia and increased mortality in patients with shock. The pooled odds ratio, represented by the diamond, lies to the right of the line of no effect (OR = 1), with confidence intervals that do not cross unity, indicating a statistically significant relationship. Most individual studies reported odds ratios greater than 1, suggesting that low serum albumin levels were associated with higher mortality risk, while a small number of studies showed results closer to the null but with wide confidence intervals that still overlapped with the overall effect. The observed heterogeneity (I^2 statistic) reflects some variability across studies, likely attributable to differences in patient populations, shock subtypes, albumin cut-off thresholds, and study designs. Despite this, the direction of effect remained

Table 4. Summary of included studies.

Study ID	Region/continent	Year of data collection	PMID	CUT OFF	Effect Type	Effect Size	95% CI	Adjusted?	Covariates adjusted for	Mortality Type	Design	Age	Male (%)
Mingjie Huang 2020 [55]	Singapore, Asia	January 2003-December 2017	30864968		OR	0.93	0.88 - 0.97	Yes – Multivariate logistic regression	ECMO duration, Preimplantation serum albumin, Preimplantation serum creatinine, Stroke and limb ischemia occurrence while on ECMO	Mortality While on ECMO	RCS	50 (21 - 70)	0.73
Mitchell Padkins 2021 [56]	Rochester, MN, USA.	2007 to 2018	33016174	3.5 g/l	OR	2.64	2.09 - 3.34	multivariable logistic regression		in hospital mortality	RCS	68.1 (57.3, 77.6)	61.5%
Razan Rabi 2024 [57]	Palestine, Middle East (Asia)	2019-2023	39196596	2,49	OR	1.88	0.9 - 3.6	Yes – Binary logistic regression	Age, Diabetes, Hypertension, Heart failure, CKD, ESRD, Liver cirrhosis, Malignancy, SOFA score, Sepsis, shock, respiratory failure, Acute kidney injury, Mechanical ventilation	in hospital mortality	RCS	54.9 (m ± 18.2)	0.6
Sang-Min Lee 2023 [58]	Seoul, Republic of Korea	January 2016 and December 2017	36652385	2.5 mg/dl	OR	2.616	1.437 - 4.751	multivariate logistic regression analysis	MD	1 year mortality	RCS	MD	MD
Sha Huang 2024 [59]	China, Asia	January 2015-December 2020	39317931	40 g/l	OR	1.964	1.08 - 3.573	Multivariate logistic regression	age, sex, COPD	in hospital mortality	RCS	>60	0.62
Tae Gun Shin 2019 [60]	South Korea, Asia	February 2011-December 2016	30654592	< 3 mg/dl	OR	3.0	2.05 - 4.39	Multivariate logistic regression	Age, Gender, Malignancy, Serum albumin level, Mean arterial pressure (MAP), Heart rate, Lactate, Creatinine, SOFA score, Use of mechanical ventilation Use of vasopressors	28 day mortality	RCS	67 (iqr: 58 - 75)	0.623
Toni Jantti 2019 [61]	Europe (Multinational: Finland, Greece, Spain, Portugal, Poland, Czech Republic, France)	October 2010-December 2012	31095609	34 g/l	OR	2.9	1.2 - 7.1	Logistic regression analysis	Comorbidities (heart failure with reduced ejection fraction, ischaemic heart disease), smoking status, calcium channel blocker use, lung oedema on X-ray, body mass index, haemoglobin, NT-proBNP and CRP at baseline, presence of multi-vessel disease in primary coronary angiography	90 days mortality	PCS	66 (msd ± 12)	0.74
Tobias Schupp *et al.* 2023. [62]	Germany, Europe	July 2017-December 2019	37108536	30 g/l	HR	1.875	1.109 - 3.170	Multivariable Cox Proportional Hazards Regression	baselinecharacteristics, clinicalandlaboratorydata,	30 days mortality	PCS	74 (63 - 81)	0.622
Song-Zan Qian 2019. [63]	United States, North America	June 2001-October 2012		2.45 g/dl	HR	1.439	1.142 - 1.814	Yes – multivariable Cox regression analysis	Age, Sex, Mean arterial pressure, Severity scores (SAPS II, Elixhauser comorbidity score), Lab values (albumin, WBC, BUN, lactate, creatinine, potassium)	30-day mortality	RCS	65.0 ± 16.2	0.541
Saeid Mirzai 2024 [64]	United States, North America	January 2017-January 2020	38258654	2.8 g/dl	HR	1.52	1.01 - 2.28	Yes – multivariable Cox regression	Not explicitly detailed in full, but adjusted for clinical variables over median follow-up of 23.6 months	All-Cause Death	RCS	72 ± 13	0.566
Danfeng Ren 2025 [65]	China, Asia	2020-2023	40438354	27.85 g/L	HR	2.172	1.266 -3.727	Yes – via Cox proportional hazards models	Age, Gender, BMI, SOFA score, APACHE II score, Comorbidities (diabetes, hypertension, coronary disease, chronic liver/kidney disease, etc.), Lab results (e.g., CRP, PCT, WBC), Mechanical ventilation, Vasopressor use, ALB infusion during first 7 days	28 day mortality	RCS	58.76 ± 17.80	0.6281



(a)



(b)

Figure 2. Meta-analysis showing correlation between hypoalbuminemia and mortality. (a) Among the seven OR studies; (b) Among the four HR studies.

consistent across studies, reinforcing the robustness of the pooled estimate. Overall, these findings support hypoalbuminemia as a significant and independent predictor of mortality among patients with shock. In Figure 2(b), the four HR studies also showed a significant association, with $I^2 = 0\%$, indicating remarkable consistency.

Figure 3 shows the funnel plot of the seven included studies. This funnel plot demonstrates a relatively symmetrical distribution of effect sizes around the pooled estimate. This symmetry suggests a low likelihood of substantial publication bias. Although a few studies show wider confidence intervals, these are evenly distributed on both sides of the pooled effect, and no strong asymmetry is observed. However, given the small number of included studies, visual inspection alone has limited power to detect bias, and complementary statistical tests such as Begg's should be interpreted alongside the funnel plot. Overall, the plot indicates

that the association between hypoalbuminemia and mortality in shock is unlikely to be driven by selective publication of positive findings.

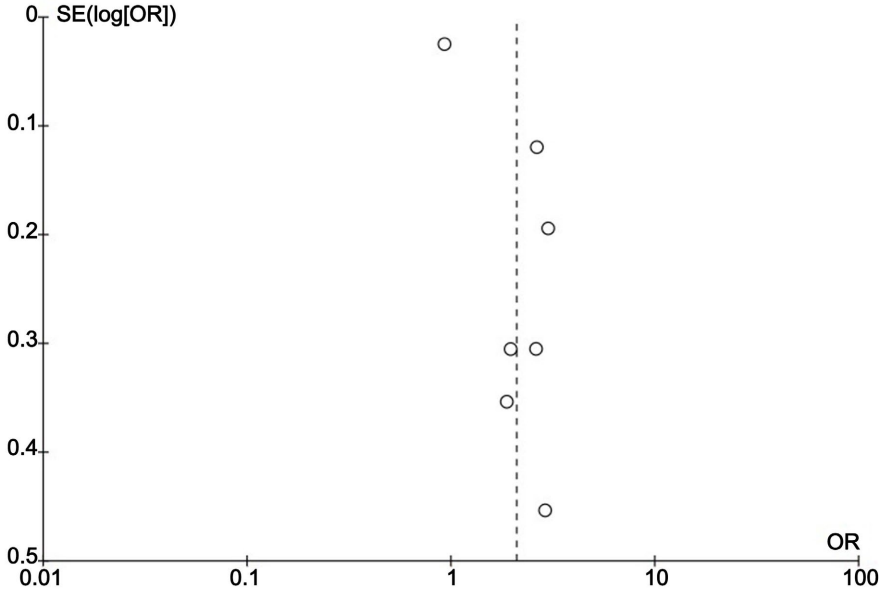


Figure 3. Funnel plot of 7 studies.

Publication Bias Assessment (Begg's Test)

Publication bias was evaluated using Begg's rank correlation test, which was conducted on the log-transformed odds ratios and their standard errors from the seven included studies. The test did not indicate significant small-study effects, with Kendall's $\tau = 0.14$, $p = 0.458$. These findings suggest no strong evidence of publication bias among the included studies when assessed by Begg's method.

To explore the very high heterogeneity ($I^2 = 95\%$) observed in the odds ratio pool, prespecified subgroup analyses were performed based on serum albumin threshold and study region. The results are summarized in Table 5.

Table 5. Subgroup analyses to address heterogeneity.

Subgroup	Pooled OR	95% CI	I^2 (%)
Albumin cutoff < 35 g/L	2.45	1.70 - 3.53	62
Other/unspecified cutoff	1.38	0.92 - 2.06	44
Asian studies	2.62	1.74 - 3.94	—
European/North American studies	1.41	0.96 - 2.07	—

The prespecified subgroup analyses provide insight into the sources of heterogeneity ($I^2 = 95\%$) observed in the overall odds ratio pool. Studies that applied a serum albumin cutoff of <35 g/L showed a markedly stronger and more consistent association between hypoalbuminemia and mortality, with substantially reduced heterogeneity ($I^2 = 62\%$). By contrast, studies with lower or unspecified thresholds

reported weaker associations and overlapping confidence intervals. Regional differences were also notable: Asian cohorts demonstrated a larger effect size (pooled OR = 2.62) compared to European and North American cohorts (pooled OR = 1.41). These findings suggest that both methodological choices (albumin threshold) and population characteristics (geographic region) may explain part of the between-study variability. However, residual heterogeneity remains, underscoring that unmeasured clinical or methodological differences likely contribute further to inconsistency.

Hartung-Knapp Adjustment on the pooled OR are presented in Table 6. In our 7-study dataset, the conventional random-effects pooled effect was OR = 2.10 (95% CI 1.20 - 3.68), while the Hartung-Knapp adjusted summary was OR = 2.10 (95% CI 1.41 - 3.13). The Hartung-Knapp adjustment did not change the statistical conclusion (association remained significant).

Table 6. Hartung-Knapp adjustment on the pooled OR.

Model	Pooled OR	95% CI	Significant vs OR = 1?
Random-effects (DL, normal CI)	2.10	1.20 - 3.69	Yes
Random-effects (DL + Hartung-Knapp)	2.10	1.41 - 3.13	Yes

Did the conclusion change under Hartung-Knapp? No.

Table 7 presents the results of leave-one-out sensitivity analyses using both the DerSimonian-Laird estimator and the Hartung-Knapp adjustment. Sequential exclusion of individual studies did not materially alter the overall pooled effect estimates, although Hartung-Knapp yielded wider confidence intervals with p-values closer to the 0.05 threshold in some cases. Confirming the robustness of findings (Table 7).

Table 7. Sensitivity analyses: DerSimonian-Laird vs Hartung-Knapp.

Excluded Study	Effect Type	DerSimonian-Laird Estimator	Hartung-Knapp Adjustment	I^2 (%)
Mingjie Huang 2020	OR	2.60 [2.19 - 3.08], P < 0.00001	2.60 [2.23 - 3.03], P < 0.0001	0
Mitchell Padkins 2021	OR	2.01 [1.10 - 3.67], P = 0.02	2.01 [1.24 - 3.26], P = 0.01	92
Razan Rabi 2024	OR	2.14 [1.16 - 3.95], P = 0.02	2.14 [1.32 - 3.48], P = 0.01	96
Sang-Min Lee 2023	OR	2.03 [1.11 - 3.73], P = 0.02	2.03 [1.26 - 3.28], P = 0.01	96
Sha Huang 2024	OR	2.13 [1.15 - 3.95], P = 0.02	2.13 [1.30 - 3.47], P = 0.01	96
Tae Gun Shin 2019	OR	1.97 [1.09 - 3.56], P = 0.02	1.97 [1.24 - 3.12], P = 0.01	95
Toni Jantti 2019	OR	2.02 [1.11 - 3.66], P = 0.02	2.02 [1.27 - 3.21], P = 0.01	96
Danfeng Ren 2025	HR	1.51 [1.25 - 1.82], P < 0.0001	1.51 [1.16 - 1.96], P = 0.02	0
Saeid Mirzai 2024	HR	1.62 [1.28 - 2.05], P < 0.0001	1.62 [0.98 - 2.69], P = 0.05	16
Song-Zan Qian 2019	HR	1.77 [1.34 - 2.33], P < 0.0001	1.77 [1.12 - 2.79], P = 0.03	0
Tobias Schupp 2023	HR	1.53 [1.27 - 1.85], P < 0.00001	1.53 [1.02 - 2.29], P = 0.04	0

4. Discussion

This systematic review and meta-analysis synthesizing 11 studies—seven reporting odds ratios and four reporting hazard ratios—provides strong evidence that hypoalbuminemia is independently associated with increased mortality in patients with shock. Across diverse populations, care settings, and study designs, low serum albumin consistently predicted worse outcomes, underscoring its role as a clinically relevant biomarker of risk.

4.1. Summary of Main Findings

The odds ratio-based meta-analysis demonstrated that patients with hypoalbuminemia had more than a twofold increased risk of death (pooled OR ≈ 2.1, 95% CI 1.2 - 3.7), while the hazard ratio-based meta-analysis confirmed that this elevated risk persisted over time (pooled HR ≈ 1.6, 95% CI 1.3 - 2.0). These results indicate that hypoalbuminemia is not only a cross-sectional marker of severity but also a longitudinal predictor of adverse prognosis during the trajectory of shock.

4.2. Heterogeneity and Subgroup Analyses

The odds ratio pool exhibited very high heterogeneity ($I^2 \approx 95\%$), which was only partly explained by prespecified subgroup analyses. Studies applying a serum albumin cutoff < 35 g/L showed stronger and more consistent associations (pooled OR ≈ 2.4, $I^2 = 62\%$) compared with studies using higher or unspecified thresholds (OR ≈ 1.4). Geographic differences also contributed: Asian cohorts reported larger effect sizes (OR ≈ 2.6) compared with European and North American cohorts (OR ≈ 1.4). These findings suggest that both methodological choices and population-level factors influence the strength of the association. Hazard ratio studies, in contrast, demonstrated consistently low heterogeneity ($I^2 < 20\%$), reinforcing the robustness of the prognostic signal over time.

4.3. Sensitivity and Robustness

Leave-one-out analyses confirmed that no single study disproportionately influenced the results. While the Hartung-Knapp adjustment widened confidence intervals and, in some cases, yielded p-values closer to the threshold of significance, the direction and magnitude of association remained stable, confirming robustness even in the context of a relatively small number of studies.

4.4. Publication Bias

The funnel plot for the seven odds ratio studies was relatively symmetrical, and Begg's rank correlation test ($\tau = 0.14$, $p = 0.458$) showed no significant small-study effects. This reduces the likelihood that the observed association is driven by selective publication of positive findings. Nonetheless, given the modest sample of studies, the presence of undetected bias cannot be entirely excluded.

4.5. Biological Plausibility

The association between hypoalbuminemia and poor outcomes in shock is biologically plausible. Albumin exerts multiple protective functions, including maintenance of plasma oncotic pressure, antioxidant activity, scavenging reactive oxygen species, binding of endogenous and exogenous toxins, and modulation of endothelial function [66]-[69]. In shock states, capillary leak, systemic inflammation, and impaired hepatic synthesis accelerate hypoalbuminemia, thereby amplifying circulatory instability and organ injury [70]. Thus, low albumin is both a marker of illness severity and a potential mediator of poor outcomes.

4.6. Comparison with Previous Literature

Our findings are congruent with prior smaller meta-analyses in sepsis and critical illness but extend them by isolating the shock population, incorporating recent high-quality cohorts, and dissecting sources of heterogeneity via meta-regression.

4.7. Clinical and Research Implications

The clinical implications are twofold. First, serum albumin measurement is inexpensive, widely available, and can be rapidly obtained, making it an attractive tool for early risk stratification in shock. Second, the heterogeneity observed across thresholds and populations suggests that context-specific cutoffs may be necessary to optimize prognostic accuracy. Whether albumin replacement therapy improves outcomes in hypoalbuminemic shock patients remains an open question; targeted interventional studies are warranted.

4.8. Limitations

This review has limitations. Residual confounding is possible, as not all studies adjusted for illness severity, nutritional status, comorbidities, or resuscitation strategies. The high heterogeneity in odds ratio studies reflects differences in populations, study design, and cutoffs, which may limit the precision of pooled estimates. Moreover, the relatively small number of studies increases the uncertainty around subgroup and meta-regression analyses.

5. Conclusion

In summary, this meta-analysis demonstrates that hypoalbuminemia is a strong and independent predictor of mortality in shock, supported by both odds- and hazard-based evidence. The consistency of results across analytic methods and populations reinforces the role of serum albumin as a clinically meaningful biomarker. Future studies should standardize definitions, evaluate age- and region-specific thresholds, and investigate whether therapeutic correction of hypoalbuminemia can modify outcomes.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Blumlein, D. and Griffiths, I. (2022) Shock: Aetiology, Pathophysiology and Management. *British Journal of Nursing*, **31**, 422-428. https://doi.org/10.12968/bjon.2022.31.8.422

[2] Ross, J., Murtaugh, R.J. and Moore, K. (2021) Shock I: Pathophysiology. In: *Critical Care*, Routledge, 60-61. https://doi.org/10.1201/9781315140629-33

[3] Jentzer, J.C., Burstein, B., Van Diepen, S., Murphy, J., Holmes, D.R., Bell, M.R., *et al.* (2021) Defining Shock and Preshock for Mortality Risk Stratification in Cardiac Intensive Care Unit Patients. *Circulation*: *Heart Failure*, **14**, e007678. https://doi.org/10.1161/circheartfailure.120.007678

[4] Bauer, M., Gerlach, H., Vogelmann, T., Preissing, F., Stiefel, J. and Adam, D. (2020) Mortality in Sepsis and Septic Shock in Europe, North America and Australia between 2009 and 2019—Results from a Systematic Review and Meta-Analysis. *Critical Care*, **24**, Article No. 239. https://doi.org/10.1186/s13054-020-02950-2

[5] Zweck, E., Thayer, K.L., Helgestad, O.K.L., Kanwar, M., Ayouty, M., Garan, A.R., *et al.* (2021) Phenotyping Cardiogenic Shock. *Journal of the American Heart Association*, **10**, e020085. https://doi.org/10.1161/jaha.120.020085

[6] Movahed, M.R., Soltani Moghadam, A. and Hashemzadeh, M. (2024) In Patients with Cardiogenic Shock, Extracorporeal Membrane Oxygenation Is Associated with Very High All-Cause Inpatient Mortality Rate. *Journal of Clinical Medicine*, **13**, Article 3607. https://doi.org/10.3390/jcm13123607

[7] Yang, J., Choi, K., Ko, Y., Ahn, C., Yu, C., Chun, W., *et al.* (2020) Clinical Characteristics and Predictors of In-Hospital Mortality in Patients with Cardiogenic Shock. *Circulation*: *Heart Failure*, **14**, e008141.

[8] Arias, G., Dominguez, P., Martinez, M., *et al.* (2021) Predictive Model for In-Hospital Mortality Following Cardiogenic Shock. *European Heart Journal*, **42**, ehab724.1535.

[9] Solangi, B.A., Shah, J.A., Kumar, R., Batra, M.K., Ali, G., Butt, M.H., *et al.* (2023) Immediate In-Hospital Outcomes after Percutaneous Revascularization of Acute Myocardial Infarction Complicated by Cardiogenic Shock. *World Journal of Cardiology*, **15**, 439-447. https://doi.org/10.4330/wjc.v15.i9.439

[10] Padkins, M., Kashani, K., Tabi, M., Gajic, O. and Jentzer, J.C. (2024) Association between the Shock Index on Admission and In-Hospital Mortality in the Cardiac Intensive Care Unit. *PLOS ONE*, **19**, e0298327. https://doi.org/10.1371/journal.pone.0298327

[11] Galusko, V., Wenzl, F.A., Vandenbriele, C., Panoulas, V., Lüscher, T.F. and Gorog, D.A. (2025) Current and Novel Biomarkers in Cardiogenic Shock. *European Journal of Heart Failure*, **27**, 1106-1125. https://doi.org/10.1002/ejhf.3531

[12] Fiorentino, M., Xu, Z., Smith, A., Singbartl, K., Palevsky, P.M., Chawla, L.S., *et al.* (2020) Serial Measurement of Cell-Cycle Arrest Biomarkers [TIMP-2]·[IGFBP7] and Risk for Progression to Death, Dialysis, or Severe Acute Kidney Injury in Patients with Septic Shock. *American Journal of Respiratory and Critical Care Medicine*, **202**, 1262-1270. https://doi.org/10.1164/rccm.201906-1197oc

[13] Fan, Y., Han, Q., Li, J., Ye, G., Zhang, X., Xu, T., *et al.* (2022) Revealing Potential Diagnostic Gene Biomarkers of Septic Shock Based on Machine Learning Analysis. *BMC Infectious Diseases*, **22**, Article No. 65. https://doi.org/10.1186/s12879-022-07056-4

[14] Jozwiak, M., Lim, S.Y., Si, X. and Monnet, X. (2024) Biomarkers in Cardiogenic Shock: Old Pals, New Friends. *Annals of Intensive Care*, **14**, Article No. 157.

https://doi.org/10.1186/s13613-024-01388-x

[15] Stanski, N.L., Stenson, E.K., Cvijanovich, N.Z., Weiss, S.L., Fitzgerald, J.C., Bigham, M.T., *et al.* (2020) PERSEVERE Biomarkers Predict Severe Acute Kidney Injury and Renal Recovery in Pediatric Septic Shock. *American Journal of Respiratory and Critical Care Medicine*, **201**, 848-855. https://doi.org/10.1164/rccm.201911-2187oc

[16] Patel, S.M., Lopes, M.S., Morrow, D.A., Bellavia, A., Bhatt, A.S., Butler, K.K., *et al.* (2024) Targeted Proteomic Profiling of Cardiogenic Shock in the Cardiac Intensive Care Unit. *European Heart Journal: Acute Cardiovascular Care*, **13**, 624-628. https://doi.org/10.1093/ehjacc/zuae068

[17] Peters, E.J., Frydland, M.S., Hassager, C., Bos, L.D.J., van Vught, L.A., Cremer, O.L., *et al.* (2024) Biomarker Patterns in Patients with Cardiogenic Shock versus Septic Shock. *IJC Heart & Vasculature*, **52**, Article 101424. https://doi.org/10.1016/j.ijcha.2024.101424

[18] De Simone, G., di Masi, A. and Ascenzi, P. (2021) Serum Albumin: A Multifaced Enzyme. *International Journal of Molecular Sciences*, **22**, Article 10086. https://doi.org/10.3390/ijms221810086

[19] Gremese, E., Bruno, D., Varriano, V., Perniola, S., Petricca, L. and Ferraccioli, G. (2023) Serum Albumin Levels: A Biomarker to Be Repurposed in Different Disease Settings in Clinical Practice. *Journal of Clinical Medicine*, **12**, Article 6017. https://doi.org/10.3390/jcm12186017

[20] di Masi, A. (2023) Human Serum Albumin: From Molecular Aspects to Biotechnological Applications. *International Journal of Molecular Sciences*, **24**, Article 4081. https://doi.org/10.3390/ijms24044081

[21] Pushkin, A.S., Martynov, A.V., Arutyunyan, A.V., Emanuel, V.L., Piskunov, D.P., Iakovleva, A.V., *et al.* (2023) Dynamics of Biophysical Characteristics of Albumin in Patients on Programmed Hemodialysis. *Nephrology* (*Saint-Petersburg*), **27**, 32-43. https://doi.org/10.36485/1561-6274-2023-27-3-32-43

[22] Ashraf, M.A., Shen, B., Raza, M.A., Yang, Z., Amjad, M.N., Din, G.U., Yue, L., Kousar, A., Kanwal, Q. and Hu, Y. (2025) Albumin: A Review of Market Trends, Purification Methods, and Biomedical Innovations. *Current Issues in Molecular Biology*, **47**, Article 303. https://doi.org/10.3390/cimb47050303

[23] Ward, E.S., Gelinas, D., Dreesen, E., Van Santbergen, J., Andersen, J.T., Silvestri, N.J., Kiss, J., Sleep, D., Rader, D., Kastelein, J., Louagie, E., Vidarsson, G. and Spriet, I. (2022) Clinical Significance of Serum Albumin and Implications of Fcrn Inhibitor Treatment in Igg-Mediated Autoimmune Disorders. *Frontiers in Immunology*, **13**. https://doi.org/10.3389/fimmu.2022.892534

[24] Bihari, S., Bannard-Smith, J. and Bellomo, R. (2020) Albumin as a Drug: Its Biological Effects Beyond Volume Expansion. *Critical Care and Resuscitation*, **22**, 257-265. https://doi.org/10.1016/s1441-2772(23)00394-0

[25] Sun, L., Yin, H., Liu, M., Xu, G., Zhou, X., Ge, P., *et al.* (2019) Impaired Albumin Function: A Novel Potential Indicator for Liver Function Damage? *Annals of Medicine*, **51**, 333-344. https://doi.org/10.1080/07853890.2019.1693056

[26] Rabbani, G. and Ahn, S.N. (2019) Structure, Enzymatic Activities, Glycation and Therapeutic Potential of Human Serum Albumin: A Natural Cargo. *International Journal of Biological Macromolecules*, **123**, 979-990. https://doi.org/10.1016/j.ijbiomac.2018.11.053

[27] Klinkmann, G., Waterstradt, K., Klammt, S., Schnurr, K., Schewe, J., Wasserkort, R., *et al.* (2023) Exploring Albumin Functionality Assays: A Pilot Study on Sepsis Evalu-

ation in Intensive Care Medicine. *International Journal of Molecular Sciences*, **24**, Article 12551. https://doi.org/10.3390/ijms241612551

[28] Artigas, A., Wernerman, J., Arroyo, V., Vincent, J. and Levy, M. (2016) Role of Albumin in Diseases Associated with Severe Systemic Inflammation: Pathophysiologic and Clinical Evidence in Sepsis and in Decompensated Cirrhosis. *Journal of Critical Care*, **33**, 62-70. https://doi.org/10.1016/j.jcrc.2015.12.019

[29] Wu, N., Liu, T., Tian, M., Liu, C., Ma, S., Cao, H., *et al.* (2023) Albumin, an Interesting and Functionally Diverse Protein, Varies from 'Native' to 'Effective' (Review). *Molecular Medicine Reports*, **29**, Article No. 24. https://doi.org/10.3892/mmr.2023.13147

[30] Wiedermann, C.J. (2021) Hypoalbuminemia as Surrogate and Culprit of Infections. *International Journal of Molecular Sciences*, **22**, Article 4496. https://doi.org/10.3390/ijms22094496

[31] Gorbacheva, A., Goudarzi, A., Vengsarkar, V.A., Pierre, C., Gerstmeyer, J., Oskouian, R., *et al.* (2025) The Impact of Hypoalbuminemia on Outcomes in Non-Surgically Treated Patients with Central Cord Injury. *Global Spine Journal*, **15**, 3244-3250. https://doi.org/10.1177/21925682251321835

[32] Afzal, A., Shahzaman, S., Azam, A., Ghani, U., Khawar, M., Afzal, N., *et al.* (2023) Hypoalbuminemia in COVID-19: Molecular and Mechanistic Approach. *Albus Scientia*, **2023**, 1-11. https://doi.org/10.56512/as.2023.1.e230606

[33] Moon, J.J., Kim, Y., Kim, D.K., Joo, K.W., Kim, Y.S. and Han, S.S. (2020) Association of Hypoalbuminemia with Short-Term and Long-Term Mortality in Patients Undergoing Continuous Renal Replacement Therapy. *Kidney Research and Clinical Practice*, **39**, 47-53. https://doi.org/10.23876/j.krcp.19.088

[34] Karki, S., Gajjar, R., Carlini, G., Jha, V. and Yadav, N. (2023) Association of Hypoalbuminemia with Clinical Outcomes in Patients Admitted with Acute Heart Failure. *Current Problems in Cardiology*, **48**, Article 101916. https://doi.org/10.1016/j.cpcardiol.2023.101916

[35] Page, M.J., McKenzie, J.E., Bossuyt, P.M., Boutron, I., *et al.* (2020) Updating Guidance for Reporting Systematic Reviews: Development of the PRISMA 2020 Statement. *Journal of Clinical Epidemiology*, **134**, 103-112.

[36] Page, M.J., McKenzie, J.E., Bossuyt, P.M., Boutron, I., *et al.* (2021) The PRISMA 2020 Statement: An Updated Guideline for Reporting Systematic Reviews. *Journal of Clinical Epidemiology*, **372**, n71.

[37] Hopewell, S., Boutron, I. and Moher, D. (2020) CONSORT and Its Extensions for Reporting Clinical Trials. In: *Principles and Practice of Clinical Trials*, Springer, 1-15. https://doi.org/10.1007/978-3-319-52677-5_188-1

[38] Page, M., Moher, D., Bossuyt, P., Boutron, I., Hoffmann, T., *et al.* (2020) PRISMA 2020 Explanation and Elaboration: Updated Guidance and Exemplars for Reporting Systematic Reviews. *The British Medical Journal*, **372**, n160.

[39] Elsman, E.B.M., Mokkink, L.B., Terwee, C.B., Beaton, D., Gagnier, J.J., Tricco, A.C., *et al.* (2024) Guideline for Reporting Systematic Reviews of Outcome Measurement Instruments (OMIs): PRISMA-COSMIN for OMIs 2024. *Journal of Clinical Epidemiology*, **173**, Article 111422. https://doi.org/10.1016/j.jclinepi.2024.111422

[40] Salameh, J., Moher, D., McGrath, T.A., Frank, R.A., Sharifabadi, A.D., Islam, N., *et al.* (2024) Assessing Adherence to the PRISMA-DTA Guideline in Diagnostic Test Accuracy Systematic Reviews: A Five-Year Follow-Up Analysis. *The Journal of Applied Laboratory Medicine*, **10**, 416-431. https://doi.org/10.1093/jalm/jfae117

[41] Davies, S. (2012) The Importance of PROSPERO to the National Institute for Health Research. *Systematic Reviews*, **1**, Article No. 5. https://doi.org/10.1186/2046-4053-1-5

[42] Sideri, S., Papageorgiou, S.N. and Eliades, T. (2018) Registration in the International Prospective Register of Systematic Reviews (PROSPERO) of Systematic Review Protocols Was Associated with Increased Review Quality. *Journal of Clinical Epidemiology*, **100**, 103-110. https://doi.org/10.1016/j.jclinepi.2018.01.003

[43] Sigg, A., Zivkovic, V., Bartussek, J., Schuepbach, R.A., Ince, C. and Hilty, M.P. (2024) The Physiological Basis for Individualized Oxygenation Targets in Critically Ill Patients with Circulatory Shock. *Intensive Care Medicine Experimental*, **12**, Article No. 72. https://doi.org/10.1186/s40635-024-00651-6

[44] Luchini, C., Stubbs, B., Solmi, M. and Veronese, N. (2017) Assessing the Quality of Studies in Meta-Analyses: Advantages and Limitations of the Newcastle Ottawa Scale. *World Journal of Meta-Analysis*, **5**, 80-84. https://doi.org/10.13105/wjma.v5.i4.80

[45] Luchini, C., Veronese, N., Nottegar, A., Shin, J.I., Gentile, G., Granziol, U., *et al.* (2020) Assessing the Quality of Studies in Meta-Research: Review/Guidelines on the Most Important Quality Assessment Tools. *Pharmaceutical Statistics*, **20**, 185-195. https://doi.org/10.1002/pst.2068

[46] Nakou, A., Dragioti, E., Bastas, N., Zagorianakou, N., Kakaidi, V., Tsartsalis, D., *et al.* (2025) Loneliness, Social Isolation, and Living Alone: A Comprehensive Systematic Review, Meta-Analysis, and Meta-Regression of Mortality Risks in Older Adults. *Aging Clinical and Experimental Research*, **37**, Article No. 29. https://doi.org/10.1007/s40520-024-02925-1

[47] Tanriver-Ayder, E., Faes, C., van de Casteele, T., McCann, S.K. and Macleod, M.R. (2021) Comparison of Commonly Used Methods in Random Effects Meta-Analysis: Application to Preclinical Data in Drug Discovery Research. *BMJ Open Science*, **5**, e100074. https://doi.org/10.1136/bmjos-2020-100074

[48] Viechtbauer, W. (2019) The R Package Metafor: Past, Present, and Future. https://doi.org/10.23668/psycharchives.2492

[49] Viechtbauer, W. and López-López, J.A. (2022) Location-Scale Models for Meta-Analysis. *Research Synthesis Methods*, **13**, 697-715. https://doi.org/10.1002/jrsm.1562

[50] Thompson, S.G. and Higgins, J.P.T. (2002) How Should Meta-Regression Analyses Be Undertaken and Interpreted? *Statistics in Medicine*, **21**, 1559-1573. https://doi.org/10.1002/sim.1187

[51] Higgins, J.P.T., Thomas, J., Chandler, J., Cumpston, M., Li, T., Page, M.J. and Welch, V.A. (2024) Cochrane Handbook for Systematic Reviews of Interventions (Version 6.5, Updated August 2024). https://www.training.cochrane.org/handbook

[52] Dwan, K. and Richardson, R. (2023) Launching "Methods and Statistics Tutorials": A Collection of Resources for Systematic Reviewers. *Cochrane Evidence Synthesis and Methods*, **1**, e12017. https://doi.org/10.1002/cesm.12017

[53] Xu, C. and Doi, S.A.R. (2020) Meta-Regression. In: *Statistics for Biology and Health*, Springer, 243-254. https://doi.org/10.1007/978-981-15-5032-4_11

[54] Tatas, Z., Kyriakou, E., Koutsiouroumpa, O., Seehra, J., Mavridis, D. and Pandis, N. (2024) Most Meta-Analyses in Oral Health Do Not Have Conclusive and Robust Results. *Journal of Dentistry*, **149**, Article 105309. https://doi.org/10.1016/j.jdent.2024.105309

[55] Huang, M., Ong, B.H., Hoo, A.E.E., Gao, F., Chao, V.T.T., Lim, C.H., *et al.* (2020)

Prognostic Factors for Survival after Extracorporeal Membrane Oxygenation for Cardiogenic Shock. *ASAIO Journal*, **66**, 141-145. https://doi.org/10.1097/mat.0000000000000984

[56] Padkins, M., Breen, T., Anavekar, N., Barsness, G., Kashani, K. and Jentzer, J.C. (2021) Association between Albumin Level and Mortality among Cardiac Intensive Care Unit Patients. *Journal of Intensive Care Medicine*, **36**, 1475-1482. https://doi.org/10.1177/0885066620963875

[57] Rabi, R., Alsaid, R.M., Matar, A.N., Dawabsheh, Y. and Abu Gaber, D. (2024) The Role of Serum Albumin in Critical Illness, Predicting Poor Outcomes, and Exploring the Therapeutic Potential of Albumin Supplementation. *Science Progress*, **107**, 1-16. https://doi.org/10.1177/00368504241274023

[58] Lee, S., Jo, Y.H., Lee, J.H., Hwang, J.E., Park, I., Baek, S., *et al.* (2023) Associations of the Serum Albumin Concentration and Sequential Organ Failure Assessment Score at Discharge With 1-Year Mortality in Sepsis Survivors: A Retrospective Cohort Study. *Shock*, **59**, 547-552. https://doi.org/10.1097/shk.0000000000002083

[59] Huang, S., Chen, L., Yang, N., Zhang, J., Wang, Y. and Chen, X. (2024) Relationships between Human Serum Albumin Levels and Septic Shock, In-Hospital, and Out-of-Hospital Mortality in Elderly Patients with Pneumonia in Different BMI Ranges. *Pneumonia*, **16**, Article No. 17. https://doi.org/10.1186/s41479-024-00138-8

[60] Shin, T.G., Kim, Y., Ryoo, S.M., Hwang, S.Y., Jo, I.J., Chung, S.P., *et al.* (2019) Early Vitamin C and Thiamine Administration to Patients with Septic Shock in Emergency Departments: Propensity Score-Based Analysis of a Before-and-After Cohort Study. *Journal of Clinical Medicine*, **8**, Article 102. https://doi.org/10.3390/jcm8010102

[61] Jäntti, T., Tarvasmäki, T., Harjola, V., Parissis, J., Pulkki, K., Javanainen, T., *et al.* (2019) Hypoalbuminemia Is a Frequent Marker of Increased Mortality in Cardiogenic Shock. *PLOS ONE*, **14**, e0217006. https://doi.org/10.1371/journal.pone.0217006

[62] Schupp, T., Behnes, M., Rusnak, J., Ruka, M., Dudda, J., Forner, J., *et al.* (2023) Does Albumin Predict the Risk of Mortality in Patients with Cardiogenic Shock? *International Journal of Molecular Sciences*, **24**, Article 7375. https://doi.org/10.3390/ijms24087375

[63] Qian, S.Z., Jin, D., Chen, Z.B., Ye, Y.C., Xiang, W.W., Ye, L.M. and Pan, J.Y. (2019) Hypoalbuminemia, a Novel Prognostic Factor for Prediction of Long-Term Outcomes in Critically Ill Patients with Septic Shock. *International Journal of Clinical and Experimental Medicine*, **12**, 7401-7409. https://e-century.us/files/ijcem/12/6/ijcem0093544.pdf

[64] Mirzai, S., Sarnaik, K.S., Persits, I., Martens, P., Estep, J.D., Chen, P., *et al.* (2024) Combined Prognostic Impact of Low Muscle Mass and Hypoalbuminemia in Patients Hospitalized for Heart Failure: A Retrospective Cohort Study. *Journal of the American Heart Association*, **13**, e030991. https://doi.org/10.1161/jaha.123.030991

[65] Ren, D., Dang, X., Ni, T., Zhou, J., Zhang, Z., Fu, S., *et al.* (2025) On-Treatment Serum Albumin Levels Can Predict 28-Day Mortality and Guide Albumin Infusion in Sepsis Patients. *Frontiers in Medicine*, **12**, Article 1490838. https://doi.org/10.3389/fmed.2025.1490838

[66] Belinskaia, D.A., Voronina, P.A., Shmurak, V.I., Jenkins, R.O. and Goncharov, N.V. (2021) Serum Albumin in Health and Disease: Esterase, Antioxidant, Transporting and Signaling Properties. *International Journal of Molecular Sciences*, **22**, Article 10318. https://doi.org/10.3390/ijms221910318

[67] Belinskaia, D.A., Voronina, P.A., Shmurak, V.I., Vovk, M.A., Batalova, A.A., Jenkins,

R.O., *et al.* (2020) The Universal Soldier: Enzymatic and Non-Enzymatic Antioxidant Functions of Serum Albumin. *Antioxidants*, **9**, Article 966. https://doi.org/10.3390/antiox9100966

[68] Aldecoa, C., Llau, J.V., Nuvials, X. and Artigas, A. (2020) Role of Albumin in the Preservation of Endothelial Glycocalyx Integrity and the Microcirculation: A Review. *Annals of Intensive Care*, **10**, Article No. 85. https://doi.org/10.1186/s13613-020-00697-1

[69] Manolis, A.A., Manolis, T.A., Melita, H., Mikhailidis, D.P. and Manolis, A.S. (2022) Low Serum Albumin: A Neglected Predictor in Patients with Cardiovascular Disease. *European Journal of Internal Medicine*, **102**, 24-39. https://doi.org/10.1016/j.ejim.2022.05.004

[70] Abedi, F., Zarei, B. and Elyasi, S. (2024) Albumin: A Comprehensive Review and Practical Guideline for Clinical Use. *European Journal of Clinical Pharmacology*, **80**, 1151-1169. https://doi.org/10.1007/s00228-024-03664-y