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Exploring the Cost-Effectiveness of Albumin-Enhanced IV Crystalloids in Sepsis Fluid Resuscitation

[1]Mohamed Metwally Mosly, [2]Hesham Metwalli Mousli, [3]Iman Mohamed Momtaz Ahmed and [4]Mohamed Ibrahim Affify Abdou

[1]Department of Pharmacy Practice – College of Pharmacy – Arab Academy for Science, Technology & Maritime Transport (AASTMT), Alexandria – Egypt.

[2]PhD. Biomedical Informatics and Medical Statistics Alexandria University, Alexandria – Egypt, Adjunct lecturer of Pharmacy Practice – College of Pharmacy – Arab Academy for Science, Technology & Maritime Transport. (AASTMT), Alexandria – Egypt.

[3]HOD of Clinical Pharmacy at Andalusia Hospital, Alexandria – Egypt.

[4]Associate Professor of Critical Care Medicine – Faculty of Medicine – Cairo University, Cairo – Egypt.

Emails: muhammadmetwally@aast.edu, heshammousli@adj.aast.edu, dr.eman.momtaz9@gmail.com, mohamedafify74@gmail.com.

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ABSTRACT:

Background: *This study aims to evaluate the cost-effectiveness of using albumin as well as crystalloids compared to the baseline use of crystalloids alone in the management of sepsis in the context of the Egyptian healthcare system. This is crucial for healthcare policymakers and managers, particularly in settings where reasonable cost containment is a priority.*

Methods: *A decision tree model was created using TreeAge Healthcare Pro software to compare two treatment groups for patients with severe sepsis or septic shock: One receiving only crystalloid fluids and the other receiving both crystalloid fluids and human albumin. The treatments were compared using the Incremental Cost-Effectiveness Ratio (ICER) and Net Monetary Benefit (NMB). Deterministic and probabilistic sensitivity analyses were conducted to assess the robustness of the results.*

Results: *Although comparing the cost-effectiveness of both alternatives showed an ICER of 162,00 L.E in favor of the albumin plus crystalloids use in sepsis cases management, there was no dominance of either alternative over the other in terms of the cost-effectiveness plane. By considering the NMB relevant to each individual alternative, the albumin plus crystalloids choice resulting in (-323,485 L.E) while the use of crystalloids alone resulting in higher NMB estimate of (-312,285 L.E). The results showed a considerable sensitivity to the cost of Albumin, the probabilistic sensitivity analysis showed robustness of the base case results over the estimated willingness to pay threshold of 160,000 L.E.*

Conclusions: *The study showed that albumin-based management of sepsis and septic shocK patients is not a cost-effective choice up to the WTP threshold of 300,000 L.E.*

KEYWORDS:

Sepsis, Cost-Effectiveness, Albumin, Fluid, Egypt, Adult

Study Findings Impact on Practice

1. **Policymakers Guidance:** The study provides guidance for policymakers on prioritizing cost-effective healthcare interventions under Egyptian universal health insurance.
2. **Resource Efficiency:** It helps allocate resources effectively by directing funds towards interventions offering the most significant health benefits per cost unit.
3. **Equitable Healthcare Access:** Ensures equitable access to essential healthcare services for all Egyptians, irrespective of socio-economic factors through utilizing an evidence-based approach.

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4. **Health Outcome Improvement:** Implementation of cost-effective interventions in ICU, such as the one identified in this study could lead to improved population health outcomes, including reduced disease burden and increased life expectancy.

1. Introduction

Sepsis, a life-threatening condition caused by the body extreme response to an infection, is characterized by an aberrant and deregulated host response leading to multiorgan dysfunction.[1,2] It poses a significant challenge in healthcare, particularly in intensive care units (ICUs).[3] The management of septic shock, a severe form of sepsis characterized by refractory hypotension or hyperlactatemia [4], remains a critical concern, with mortality rates varying based on the setting and severity of the disease, reaching up to 80% for cases of septic shock.[5-7]

The fluid therapy, which represents a core component of septic shock management, involves the use of crystalloids and colloids, with the latter including human albumin. The debate over the use of colloids, particularly albumin, originates from the contrasting findings regarding its mortality benefits in sepsis cases management. While some studies, like the Saline Versus Albumin Fluid Evaluation trial and the Albumin Italian Outcome Sepsis (ALBIOS) trial, suggest a mortality reduction benefit with albumin use in septic shock[8,9], others indicated no significant mortality reduction.[10,11] In countries like Egypt, where healthcare resources are often limited, the cost-effectiveness of treatments like albumin becomes especially pertinent. The economic evaluation of fluid therapy in sepsis patients, including the use of albumin, has not been given significant attention despite its potential to influence healthcare expenditure and policy decisions.[9] This is critical given the expensive nature of albumin, which can significantly inflate healthcare costs if prescribed indiscriminately.[9]

Given this background, the study at hand aims to evaluate the cost-effectiveness of using albumin as well as crystalloids compared to the baseline use of crystalloids alone in the management of sepsis in the context of the Egyptian healthcare system. This evaluation is crucial for healthcare policymakers and managers, particularly in settings where reasonable cost containment is a priority. By focusing on the cost-effectiveness of albumin in sepsis management, this study seeks to contribute valuable insights into optimizing healthcare resources and improving patient outcomes in Egypt and similar settings which are undergoing significant transformations with the impending implementation of the universal health insurance system.

2. Methods

2.1. Decision Analysis Model

A decision tree model was created using TreeAge, LLC (Healthcare Pro® Version 2023 R2.0) software. The model was based on a hypothesized group of patients with either severe sepsis or septic shock. These patients were divided into two groups based on the type of fluids administered for management: crystalloid fluids only or a combination of crystalloid fluids and human albumin. The model tracked these patients from the onset of severe sepsis or septic shock, up to a duration of 28 days.[8] The researchers developed the model from the perspective of healthcare systems, such as universal health insurance authorities, and each treatment pathway within the model indicated the likelihood of survival or mortality within 28 days.[8] They did not incorporate potential negative side effects from the treatments into this model. Figure 1 displays the decision tree model constructed for comparing the alternative basic estimates,

2.2. Model Inputs

2.2.1. Cost data

The cost analysis included standard care costs for severe sepsis and septic shock, determined using the Delphi consensus approach to obtain as accurate data as possible regarding the direct medical costs attributed to the management regimen of sepsis patients in the compared alternatives, including both ICU and ward hospital stays. The Delphi approach involved two successive rounds of surveying a panel of experts to achieve the maximum consensus level. [12-14] The final reported cost data demonstrated a high level of agreement, confirmed by conducting Intraclass Correlation testing, which yielded above 90% reliability in both averages and ranges of input values.[15,16] All costs are reported in terms of the 2023 Egyptian pound currency (L.E), as all costs were reported for a timeframe of less than one year, requiring no cost adjustments. **Table 1** presents descriptive values for each cost item used in the analysis, along with their reported ranges.

Table 1. Estimates of cost-effectiveness model input parameters and their assigned probability distributions

Input Parameter Name	Minimum value	Input parameter base case value (average)	Maximum value	Distribution
Cost of Albumin	14400	16200	18000	Gamma
Cost of Anaerobic Culture	191	325	460	Gamma
Cost of Antibiotics	20570	49640	69020	Gamma
Cost of Blood Culture	408	790	1170	Gamma
Cost of Hemodialysis (HD)	4050	21000	36000	Gamma
Cost of ICU Stay	80000	240000	400000	Gamma
Cost of Mechanical Ventilation (MV)	7200	11100	15000	Gamma
Cost of Sputum Culture	95	215	335	Gamma
Cost of Urine Culture	95	215	335	Gamma
Cost of Ward Stay	28000	84000	140000	Gamma
Probability of Mortality with Crystalloids	0.43	0.52	0.61	Beta
Probability of Mortality with Crystalloids plus Albumin	0.37	0.5	0.52	Beta
Life Years Gained with Crystalloids	1.64	1.9	2.3	Gamma
Life Years Gained with Crystalloids plus Albumin	1.9	2	2.7	Gamma

2.2.2. Outcome data

2.2.2.1. Mortality data

Probabilities of mortality for both decision arms were derived from Tigabu et al.'s study.[17] The study used the odds ratio for mortality, derived from a meta-analysis of clinical trials,[18] to calculate the probabilities of 28-day survival with and without the addition of albumin. These probabilities were then integrated into the decision tree model. The odds ratio was converted into a probability of mortality for patients treated with albumin and crystalloids.[17]

2.2.2.1. Life Years Gained

The main outcome data were expressed in terms of Life Years Gained (LYG). Data for life expectancy years gained were also utilized from the Tigabu et al.'s study.[17] They developed Life Years Gained for either choice using the Declining Exponential Average Life Expectancy (DEALE) method. This approach considered life expectancy for the general population at a given age and the mortality rate for each treatment group.[19]

2.3. Base Case Cost-Effectiveness Analysis

The cost-effectiveness of the compared alternative approaches for managing sepsis was evaluated using the Incremental Cost-Effectiveness Ratio (ICER), which represents the incremental cost per additional life year gained from one treatment compared to another. Additionally, the Net Monetary Benefit (NMB) was calculated to provide a more standardized method for comparing the value of benefits gained from implementing either alternative. This allows for determining which choice is more cost-effective.[20]

2.4. Sensitivity Analyses

2.4.1. Deterministic sensitivity analysis

To assess the robustness of the proposed model, a deterministic sensitivity analysis was performed by evaluating the robustness of the results reached upon varying the values of each single model parameter along its respective range.[21] The respective ranges were obtained from the results of Delphi consensus approach for the Cost data,[15,16] and from the literature for the outcome data.[17] the results of the deterministic sensitivity analysis were reported in terms of a Tornado diagram.

2.4.2. Probabilistic sensitivity analysis

The researchers employed the Monte Carlo simulation approach for conducting probabilistic sensitivity analysis, allowing all model input parameters to vary simultaneously according to their respective probability distributions.[21] The cost data and the values for life years gained were assigned a Gamma distribution, while the probabilities of mortality were assigned a Beta distribution. To draw the final conclusions of the study, this probabilistic sensitivity analysis was set to run one thousand iterations. A cost-effectiveness acceptability curve (CEAC) was constructed to illustrate the likelihood of choosing cost-effectiveness in relation to a willingness-to-pay (WTP) value ranging from 50,000 to 500,000 Egyptian Pounds (L.E). The researchers have conservatively estimated the exact WTP value for this study to be 160,000 L.E, equivalent to 1.5 times the country national GDP per capita.[22,23]

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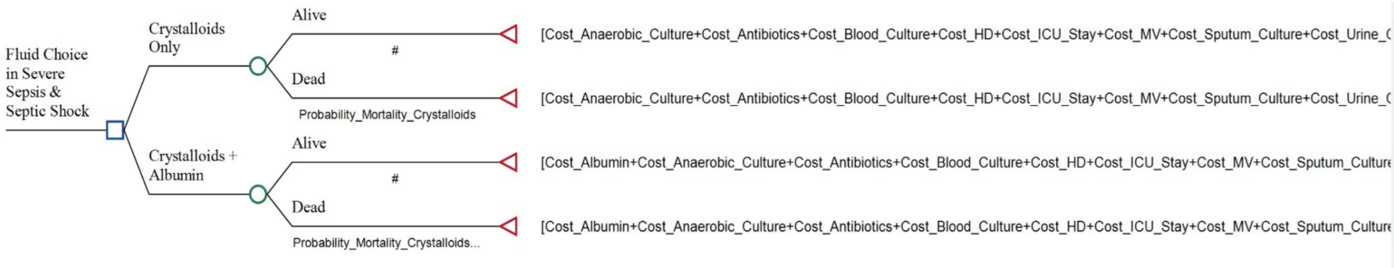

Figure 1. Decision tree model for estimating the cost-effectiveness results for base-case scenario

3. Results

3.1. Base Case Cost-effectiveness Results

Although comparing the cost-effectiveness of both alternatives showed an ICER i.e., the cost of each extra life year gained to be 162,000 L.E for the albumin plus crystalloids use in sepsis cases management, there was no dominance of either alternative over the other in terms of the cost-effectiveness plane showed in **figure 2**. This finding can be totally reversed by considering the NMB relevant to each individual alternative at a WTP of 160,000 L.E. Having the albumin plus crystalloids choice resulting in (-323,485 L.E) while the use of crystalloids alone resulting in higher NMB estimate of (-312,285 L.E), the researchers can clearly conclude that the baseline use of crystalloids alone is more cost-effective than the use of albumin as well as crystalloids in the management of sepsis cases. Results of the base case analysis are shown in **table 2**.

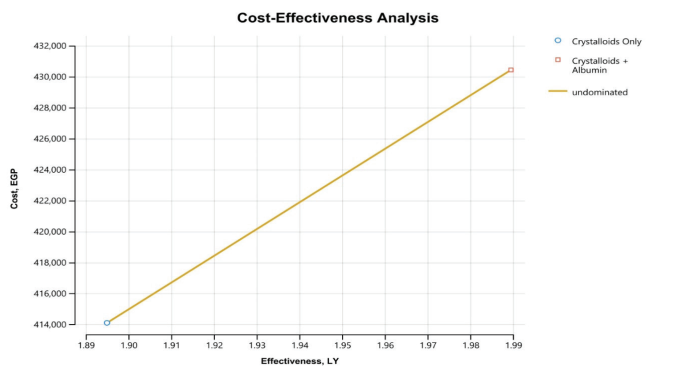

Figure 2. Cost-effectiveness plane for the base-case scenario comparison

*Cost in Egyptian pounds (L.E).

*Effectiveness in life years (LY) gained.

Table 2. Base case results for the Cost-Effectiveness decision tree model

Strategy	Dominance	Cost	Incr. Cost (L.E)	Eff.	Incr. Eff. (LYG)	ICER (L.E/LYG)	NMB
Baseline Crystalloids	Undominated	407,285		1.9			-312,285
Crystalloids plus Albumin	Undominated	423,485	16,200	2	0.1	162,000	-323,485

3.2. Deterministic Sensitivity Analysis Results

The one-way sensitivity analysis presented by the tornado diagram has revealed consistent results upon varying each input individually except for the cost of Albumin. The results were considerable sensitivity to the changes in Albumin cost, this can be clearly noticed in the Tornado diagram displayed in **figure 3**.

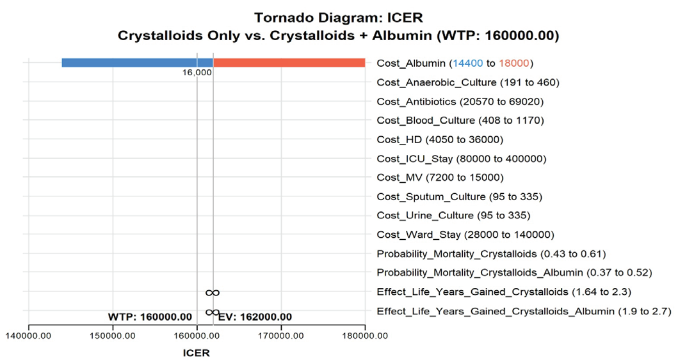

Figure 3. Tornado diagram showing results of the deterministic sensitivity analysis

*WTP: Willingness to Pay *EV: Estimated Value

3.3. Probabilistic Sensitivity Analysis Results

The Monte Carlo simulation results were reported in form of the Incremental Cost-Effectiveness (ICE) scatterplot encompassing the simultaneously varying inputs effect on the ICE outcome for the tested 1,000 different iterations. The higher portion of the iteration under the estimated Egyptian Willingness to Pay (WTP) of 16,000 L.E were in favor of the baseline use of crystalloids alone indicating that it is more cost-effective. This can be further illustrated using the Cost-Effectiveness Acceptability Curve (CEAC) displayed in **figure 4**. Upon observing the directions shown in the Cost-Effectiveness Acceptability Curve CEAC, the researchers can realize that that Cost-Effectiveness status turns in favor of using albumin as well as crystalloids when Willingness to Pay (WTP) comes into about two times the current estimated Egyptian WTP threshold.

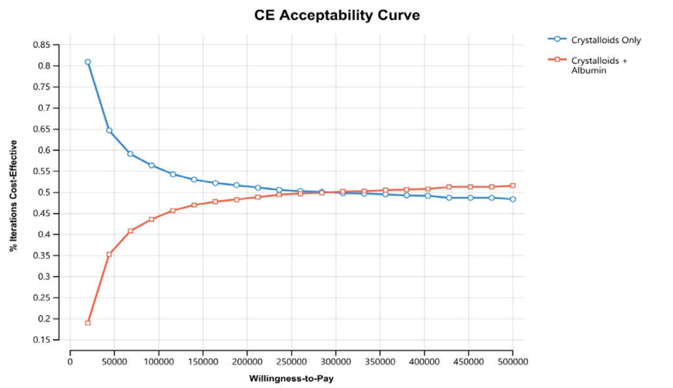

Figure 4. Cost-Effectiveness Acceptability Curve (CEAC)

4. Discussion

It is well-known that the administration of intravenous (IV) fluids is a fundamental aspect of managing sepsis patients in the intensive care unit (ICU). Approximately two-thirds of sepsis patients respond well to fluid resuscitation during the early stages of sepsis.[24,25] The administration of IV fluids should continue alongside continuous improvements in the patient's hemodynamic parameters, such as stroke volume and cardiac output.[26]

While the use of crystalloids in fluid resuscitation is recommended by the 2021 Sepsis Campaign guidelines, the use of albumin as a resuscitation fluid in sepsis remains controversial. Despite this, albumin is employed due to its ability to support oncotic pressure and thus maintain intravascular volume.[27,28]

The present study revealed that the use of human albumin as an add on to the baseline crystalloids use in managing sepsis cases was not cost-effective on the basic case scenario developed by the decision tree model utilizing the WTP of 160,000 L.E that is equivalent to 1.5 times the Egyptian GDP per capita for each life year gained.

The choice of using human albumin as well as crystalloids showed a NMB of (-323,485 L.E), while the standard choice of crystalloids alone showed a NMB of (-312,285 L.E). Upon deterministic sensitivity analysis conduction, the results reached showed robustness over the compared ranges of input parameters except that for the albumin cost. These results came in contrary with that for the study published in 2014 to evaluate the cost-effectiveness of fluids resuscitation alternatives for managing severe sepsis patients based on reviewing recent clinical trials that showed the cost-effectiveness of albumin-based management in severe sepsis and septic shock cases.[29] This contradictory results may be attributed to the major difference in albumin accessibility and hence affordability in the Egyptian market from the US healthcare system that can guarantee more accessibility and affordability of albumin. On the other hand, when looking at a similar study that was conducted in Iran, one can realize that this study results came in alignment with its results that revealed the baseline crystalloids management choice as the cost-effective one.[9] The consistency in these results with the Iranian study is thought to be due to similarity in healthcare market systems. In a recent multicenter study conducted in Jordan, the results of exploring the cost-effectiveness analysis for both alternatives have showed that albumen use was not a cost-effective choice from the Jordanian healthcare system perspective.[30] This can considerably support the current study findings due to similarity in Egyptian and Jordanian economic status as both are categorized among the Low- and Middle-Income Countries (LMICs).
Building on the probabilistic sensitivity analysis results, the researchers found that the baseline treatment using only crystalloids is a cost-effective choice over a wide range of probabilities, with a willingness-to-pay (WTP) threshold up to 300,000 L.E. Beyond this WTP threshold, there is a gradual yet trivial increase in favor of albumin-based management. This pattern is somewhat consistent with the probabilistic sensitivity analysis from a recent multicenter Jordanian study.[30] Meanwhile, when comparing the reached results to those of the French COOAST study, which evaluated the cost-effectiveness of albumin in severe sepsis and septic shock cases, a clear difference emerges. The French study confidently concludes that albumin-based management is always the cost-effective choice.[31]

Although not being included in the list of specific Diagnosis Related Group (DRG) of specific medications that necessitates specific reimbursement, the cost of whatever used albumin quantity, albumin-based management remains the cost-effective choice according to French COOAST study. This may be explained by the relative robustness of the French economic system.[31,32]

5. Strengths of the Study

The present study came as a trial to fill the gap in examining the cost-effectiveness of one of the crucial healthcare provided services that has a great burden on the Egyptian national level. The reseachers tried their best to use model parameters that cover most of the Egyptian real-world situation.

6. Limitations of the Study

One of the main limitations in the present study resides with the deficient national exact estimates of the outcome data. The reserachers believe that conduction of prospective multicenter national studies is of a great positive impact specially that it

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guarantees a more comprehensive data collection methods in a multitude of different settings and patient rates.

7. Conclusions

The present study has demonstrated that albumin-based management of patients with sepsis and septic shock is not a cost-effective option up to the willingness-to-pay (WTP) threshold of 300,000 L.E. This finding underscores the importance of evaluating the cost-effectiveness of healthcare interventions, especially in the context of implementing the Egyptian Universal Health Insurance. The researchers strongly recommend conducting further studies to optimize the healthcare services provided. It would be extremely beneficial for national policymakers to consider these evaluations when developing a national Diagnosis Related Group (DRG) system, which is crucial for designing an appropriate reimbursement system.

List of Abbreviations

ICUs	Intensive Care Units
L.E	Egyptian pound
DEALE	Declining Exponential Average Life Expectancy
ICER	Incremental Cost-Effectiveness Ratio
EFF	This is crucial for
NMB	Net Monetary Benefit
CEAC	Cost-Effectiveness Acceptability Curve
WTP	Willingness-to-Pay
ICE	Incremental Cost-Effectiveness
IV	Intravenous
LMICs	Low- and Middle-Income Countries
DRG	Diagnosis Related Group

Declarations

1.1. Ethics approval and consent to participate
The study is an economic evaluation and does not involve experiments on humans and/or the use of human tissue samples.

1.2. Consent for publication
'Not applicable'

1.3. Availability of data and materials
All data generated or analyzed during this study are included in this published article [and its supplementary information files].

1.4. Competing interests
'Not applicable'

1.5. Funding
'Not applicable'

1.6. Authors' contributions
MM conducted the economic analysis and revised from the clinical pharmacy expert's point of view.
HM generated the idea, conducted the literature review, and the scientific writing of the manuscript.
IM collected and reviewed the data, shared in Delphi technique approach conduction.
MA reviewed the manuscript from the clinical expert's point of view, shared in the Delphi technique conduction.

1.7. Acknowledgements
'Not applicable'

1.8. Footnotes
'Not applicable'

8. REFERENCES

1. Howell MD, Davis AM. Management of Sepsis and Septic Shock. JAMA. 2017 Feb 28;317(8):847.

2. Singer M, Deutschman CS, Seymour C, Shankar-Hari M, Annane D, Bauer M, et al. The third international consensus definitions for sepsis and septic shock (sepsis-3). Vol. 315, JAMA - Journal of the American Medical Association. 2016.

3. Vincent JL, Marshall JC, Ñamendys-Silva SA, François B, Martin-Loeches I, Lipman J, et al. Assessment of the worldwide burden of critical illness: The Intensive Care Over Nations (ICON) audit. Lancet Respir Med. 2014;2(5).

4. Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, et al. Surviving Sepsis Campaign. Crit Care Med. 2013 Feb;41(2):580–637.

5. Jawad I, Lukšić I, Rafnsson SB. Assessing available information on the burden of sepsis: Global estimates of incidence, prevalence and mortality. J Glob Health. 2012;2(1).

6. Angus DC, van der Poll T. Severe Sepsis and Septic Shock. New England Journal of Medicine. 2013 Aug 29;369(9):840–51.

7. Mayr FB, Yende S, Angus DC. Epidemiology of severe sepsis. Vol. 5, Virulence. 2014.

8. Finfer S, McEvoy S, Bellomo R, McArthur C, Myburgh J, Norton R, et al. Impact of albumin compared to saline on organ function and

mortality of patients with severe sepsis. Intensive Care Med. 2011;37(1).

9. Caironi P, Tognoni G, Masson S, Fumagalli R, Pesenti A, Romero M, et al. Albumin Replacement in Patients with Severe Sepsis or Septic Shock. New England Journal of Medicine. 2014;370(15).

10. Jiang L, Jiang S, Zhang M, Zheng Z, Ma Y. Albumin versus other fluids for fluid resuscitation in patients with sepsis: A meta-analysis. PLoS One. 2014;9(12).

11. Patel A, Laffan MA, Waheed U, Brett SJ. Randomised trials of human albumin for adults with sepsis: systematic review and meta-analysis with trial sequential analysis of all-cause mortality. BMJ. 2014 Jul 22;349(jul22 10):g4561–g4561.

12. Keeney S, Hasson F, Mckenna H. The Delphi Technique in Nursing and Health Research. The Delphi Technique in Nursing and Health Research. 2010.

13. Fayanju OM, Haukoos JS, Tseng JF. CHEERS Reporting Guidelines for Economic Evaluations. Vol. 156, JAMA Surgery. 2021.

14. Tchouaket Nguemeleu E, Boivin S, Robins S, Sia D, Kilpatrick K, Brousseau S, et al. Development and validation of a time and motion guide to assess the costs of prevention and control interventions for nosocomial infections: A Delphi method among experts. PLoS One. 2020 Nov 12;15(11):e0242212.

15. Birko S, Dove ES, Özdemir V, Dalal K. Evaluation of nine consensus indices in delphi foresight research and their dependency on delphi survey characteristics: A simulation study and debate on delphi design and interpretation. PLoS One. 2015;10(8).

16. Niederberger M, Köberich S. Coming to consensus: The Delphi technique. European Journal of Cardiovascular Nursing. 2021;20(7).

17. Tigabu B, Davari M, Kebriaeezadeh A, Mojtahedzadeh M, Sadeghi K, Jahangard-Rafsanjani Z. Is Albumin-based Resuscitation in Severe Sepsis and Septic Shock Justifiable? An Evidence from a Cost-effectiveness Evaluation. Ethiop J Health Sci. 2019;29(1).

18. Xu JY, Chen QH, Xie JF, Pan C, Liu SQ, Huang LW, et al. Comparison of the effects of albumin and crystalloid on mortality in adult patients with severe sepsis and septic shock: A meta-analysis of randomized clinical trials. Crit Care. 2014;18(6).

19. Beck JR, Pauker SG, Gottlieb JE, Klein K, Kassirer JP. A convenient approximation of life expectancy (the "DEALE"). II. Use in medical decision-making. Am J Med. 1982;73(6).

20. Zethraeus N, Johannesson M, Jönsson B, Löthgren M, Tambour M. Advantages of using the net-benefit approach for analysing uncertainty in economic evaluation studies. Vol. 21, PharmacoEconomics. 2003.

21. Vreman RA, Geenen JW, Knies S, Mantel-Teeuwisse AK, Leufkens HGM, Goettsch WG. The Application and Implications of Novel Deterministic Sensitivity Analysis Methods. Pharmacoeconomics. 2021;39(1).

22. Iino H, Hashiguchi M, Hori S. Estimating the range of incremental costeffectiveness thresholds for healthcare based on willingness to pay and GDP per capita: A systematic review. Vol. 17, PLoS ONE. 2022.

23. Bank W. GDP (current US) | Data [Internet]. 2010. Available from: https://data.worldbank.org/indicator/NY.GDP.MKTP.CD?locations=EG

24. Dellinger RP, Carlet JM, Masur H, Gerlach H, Calandra T, Cohen J, et al. Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock. Crit Care Med. 2004 Mar;32(3):858–73.

25. Leisman DE, Doerfler ME, Schneider SM, Masick KD, D'Amore JA, D'Angelo JK. Predictors, prevalence, and outcomes of early crystalloid responsiveness among initially hypotensive patients with sepsis and septic shock. Crit Care Med. 2018;46(2).

26. Cecconi M, De Backer D, Antonelli M, Beale R, Bakker J, Hofer C, et al. Consensus on circulatory shock and hemodynamic monitoring. Task force of the European Society of Intensive Care Medicine. Intensive Care Med. 2014;40(12).

27. Evans L, Rhodes A, Alhazzani W, Antonelli M, Coopersmith CM, French C, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. Intensive Care Med. 2021 Nov 2;47(11):1181–247.

28. Melia D, Post B. Human albumin solutions in intensive care: A review. Vol. 22, Journal of the Intensive Care Society. 2021.

29. Farrugia A, Bansal M, Balboni S, Kimber M, Martin G, Cassar J. Choice of Fluids in Severe Septic Patients - A Cost-effectiveness Analysis Informed by Recent Clinical Trials.

Advances in Medical, Pharmaceutical and Dental Research Journal (AMPDR)- ISSN 2812-4898
http://dx.doi.org/10.21622/AMPDR.2024.04.2.914

Rev Recent Clin Trials. 2014;9(1).

30. Altawalbeh SM, Almestarihi EM, Khasawneh RA, Momany SM, Abu Hammour K, Shawaqfeh MS, et al. Cost-effectiveness of intravenous resuscitation fluids in sepsis patients: a patient-level data analysis in Jordan. J Med Econ. 2024 Dec 31;27(1):126–33.

31. Guidet B, Mosqueda GJ, Priol G, Aegerter P. The COASST study: Cost-effectiveness of albumin in severe sepsis and septic shock. J Crit Care. 2007;22(3).

32. Malguid C. Direction Générale du Trésor et de la Politique Économique. Analyse économique de la prévention des risques pour la santé. Diagnostics Prévisions et Analyses Économiques. 2005;(71).