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Sepsis

Current Awareness Bulletin

September 2025

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Book a session today at https://forms.office.com/e/HyiSXfDaYV (these sessions will be held on a monthly basis)

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1. **Impact of underweight status on mortality in sepsis patients: a meta-analysis.**

Authors: Chen, Jiaan;Zhang, Fan;Liang, Li;Pan, Xuming;Zhang, Jiancheng and Jin, Guangjun

Publication Date: 2025

Journal: Frontiers in Medicine 12, pp. 1549709

Abstract: Objective: The evidence regarding the impact of underweight status on clinical outcomes in patients with sepsis are still scarce and controversial. We aimed at conducting a meta-analysis to evaluate the potential associations between underweight and the mortality rate among sepsis patients. Methods: A comprehensive electronic search was performed in PubMed, Cochrane Library, Embase, and Web of Science databases. Odds ratios (ORs) or mean differences and 95% confidence intervals (CIs) were calculated using RevMan 5.3. Results: A total of 58,348 patients (normal weight group: 49,084 patients; underweight group: 9,264 patients) from 23 studies were included in this meta-analysis. The results indicated that the in-hospital mortality (OR, 1.28; 95% CI, 1.21, 1.35; heterogeneity: I 2 = 21%, P = 0.21), 28-day mortality (OR, 1.54; 95% CI, 1.26, 1.88; heterogeneity: I 2 = 74%, P I 2 = 41%, P = 0.17) of underweight patients were significantly higher than those of normal weight patients. However, there was no significant difference in length of hospital stay or intensive care unit length of stay between underweight patients and normal-weight patients. Conclusion: Underweight is associated with increased mortality in patients with sepsis. Physicians should pay more attention to the management of underweight sepsis patients. Systematic review registration: https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=631417, identifier CRD42025631417. Copyright © 2025 Chen, Zhang, Liang, Pan, Zhang and Jin.

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2. **Comparison of Ibuprofen and Paracetamol for Fever Management in Sepsis and Septic Shock: A Randomized Controlled Trial.**

Authors: Donmez S.;Sener A.;Isik N.I.;Akbas I.;Mutlu R.I.;Siber V.;Yilmaz M. and Oguzturk, H.

Publication Date: 2025

Journal: Eurasian Journal of Emergency Medicine 24(2), pp. 140–147

Abstract: Aim: The aim of this study was to compare the efficacy of ibuprofen and paracetamol in fever management in patients with sepsis and septic shock and to evaluate their effects on body temperature and treatment outcomes. Material(s) and Method(s): This randomized, parallel-controlled, double-blind study was conducted at Ankara Bilkent City Hospital. Patients aged 18 years and older diagnosed with sepsis or septic shock and presenting with a fever of >=38.3 degreeC were randomly assigned to receive either intravenous ibuprofen (400 mg) or paracetamol (1 g). Body temperature was measured before treatment and at 30, 60, and 120 minutes after treatment. The primary outcomes were changes in body temperature and the proportion of patients achieving a body temperature Material(s) and Method(s): This randomized, parallel-controlled, double-blind study was conducted at Ankara Bilkent City Hospital. Patients aged 18 years and older diagnosed with sepsis or septic shock and presenting with a fever of >=38.3 degreeC were randomly assigned to receive either intravenous ibuprofen (400 mg) or paracetamol (1 g). Body temperature was measured before treatment and at 30, 60, and 120 minutes after treatment. The primary outcomes were changes in body temperature and the proportion of patients achieving a body temperature Result(s): After excluding patients with incomplete data, a total of 113 patients (64.6% female) were analyzed. Both groups demonstrated a reduction in fever at 30, 60, and 120 minutes. No significant differences were observed between the groups in demographic characteristics, clinical parameters, or severity scores (p>0.05). The most common source of infection was pulmonary, followed by urinary system infections. No significant difference in the distribution of infection sources was identified between the groups (p>0.05). Conclusion(s): Although a significant effect favoring ibuprofen was observed at 30 minutes, both ibuprofen and paracetamol effectively reduced fever in patients with sepsis and septic shock, with no significant difference in efficacy between the two drugs over time.

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3. **The Effect of Severe Sepsis and Septic Shock Management Bundle (SEP-1) Compliance and Implementation on Mortality Among Patients With Sepsis : A Systematic Review.**

Authors: Ford, James S.;Morrison, Joseph C.;Kyaw, May;Hewlett, Meghan;Tahir, Peggy;Jain, Sonia;Nemati, Shamim;Malhotra, Atul and Wardi, Gabriel

Publication Date: Apr ,2025

Journal: Annals of Internal Medicine 178(4), pp. 543–557

Abstract: BACKGROUND: The Centers for Medicare & Medicaid Services (CMS) Severe Sepsis and Septic Shock Management Bundle (SEP-1) is now included in the Hospital Value-Based Purchasing (VBP) Program. PURPOSE: To assess the evidence supporting SEP-1 compliance or SEP-1 implementation in improving sepsis mortality. DATA SOURCES: PubMed, Web of Science, EMBASE, CINAHL Complete, and Cochrane Library from inception to 26 November 2024. STUDY SELECTION: Studies of adults with sepsis that included 3- or 6-hour sepsis bundles defined by SEP-1 specifications. DATA EXTRACTION: Article screening, full-text review, data extraction, and risk-of-bias assessment were independently performed by 2 authors. Level of evidence was determined using GRADE (Grading of Recommendations Assessment, Development and Evaluation) criteria and National Quality Forum criteria. DATA SYNTHESIS: A total of 4403 unique references were screened, and 17 studies were included. Twelve studies assessed the relationship between SEP-1 compliance and mortality; 5 showed statistically significant benefit, whereas 7 did not. Among studies showing benefit, 1 did not adjust for confounders, 1 found benefit only among patients with severe sepsis, 1 included only patients with septic shock, and 1 included only Medicare beneficiaries. Five studies assessed the relationship between SEP-1 implementation and sepsis mortality; only 1 showed significant benefit, but

it did not adjust for mortality trends before SEP-1 implementation. All 17 studies were observational, and none had low risk of bias. LIMITATIONS: The conclusions are limited by the underlying quality of the available studies, as all were observational. Because there was considerable methodologic heterogeneity among the included studies, a meta-analysis was not performed as the results could have been misleading. CONCLUSION: This review found no moderate- or high-level evidence to support that compliance with or implementation of SEP-1 was associated with sepsis mortality. CMS should reconsider the addition of SEP-1 to the Hospital VBP Program. PRIMARY FUNDING SOURCE: None. (PROSPERO: CRD42023482787).

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4. **Beyond the Beat: A Multifaceted Review of Atrial Fibrillation in Sepsis: Risk Factors, Management Strategies, and Economic Impact**

Authors: Ho, Wing Lam;Umais, Muhammad;Bai, Meena;Dang, Ngoc Bao;Kumari, Kajal;Izhar, Sara;Asrar, Rabia;Haddad, Toleen and Muzammil, Muhammad Ali

Publication Date: Feb ,2025

Journal: Cardiology Research 16(1), pp. 1–14

Abstract: Atrial fibrillation (AF) is a common arrhythmia in critically ill patients. The objective of this narrative review is to evaluate the characteristics of patients who develop new-onset atrial fibrillation (NOAF) because of sepsis, current management of NOAF in sepsis patients, special consideration in different populations that developed NOAF, health economic and quality of life of patients. We conducted a literature search on PubMed to find research related to NOAF, sepsis and critical illness. Nineteen studies were analyzed for risk factors and outcomes. The incidence rate ranges from 0.53% to 43.9% among these studies. There were numerous risk factors that had been reported from these articles. The most reported risk factors included advanced age, male sex, White race, and cardiovascular comorbidities. The management of septic patients is significantly challenging because of the unfavorable cardiovascular consequences and thromboembolic hazards associated with NOAF. There are comprehensive guidelines available for managing AF, but the effectiveness and safety of therapies in patients with sepsis are still uncertain. Various approaches for managing newly diagnosed AF have been explored. Sinus rhythm can be restored through either pharmacological or non-pharmacological intervention or combination of both. In addition, thromboembolism is a complication that can occur in patients with AF and can have a negative impact on the prognosis of sepsis patients. The use of anticoagulation to prevent stroke after NOAF in sepsis patients is still controversial. Extensive prospective investigations are required to have a deeper understanding of the necessity for anticoagulation following NOAF in sepsis. Beside the treatment of NOAF, early detection of NOAF in sepsis plays a critical role. The prompt initiation of rhythm control medication following a clinical diagnosis of AF can enhance cardiovascular outcomes and reduce mortality in patients with AF and cardiovascular risk factors. Additionally, NOAF in the intensive care unit can prolong hospital stays, increasing hospitalization costs and burdening the hospital. Therefore, preventing and managing NOAF effectively not only benefit the patients but also the hospital in financial aspect. Lastly, to address the existing gaps in knowledge, future research should focus on developing machine learning models that can accurately anticipate risks, establish long-term follow-up protocols, and create complete monitoring systems. The focus is on early intervention and personalized approaches to improve outcomes and quality of life. Copyright 2025, Ho et al.

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5. **Optimal time and volume of fluid resuscitation in patients with sepsis: a nationwide multicenter cohort study.**

Authors: Hyun D.G.;Ahn J.H.;Huh J.W.;Hong S.B.;Koh Y.;Oh D.K.;Lee S.Y.;Park M.H. and Lim, C. M.

Publication Date: 2025

Journal: Scientific Reports 15(1), pp. 30465

Abstract: The optimal fluid resuscitation strategy for managing sepsis remains unknown. We aimed to

examine the independent and joint associations of infusion time and volume of fluid resuscitation on mortality in patients with sepsis. We analyzed adult patients with sepsis who received > 20 mL/kg of fluid for initial resuscitation within 6 h after the start of fluid resuscitation from prospectively collected nationwide data at 15 hospitals in South Korea between September 2019 and December 2022.The volume of administered fluid (mL/kg) was categorized into six groups (20 to = 45) and infusion time (h) was categorized into two groups (3). Among a total of 1305 patients, a fluid volume of 40 to 3). Among a total of 1305 patients, a fluid volume of 40 to 3). Among a total of 1305 patients, a fluid volume of 40 to 30%) volume of fluid than the current recommendation within 3 h was associated with a lower risk of mortality.

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6. **Association between serum anion gap trajectory and mortality in hospitalized patients with sepsis: an analysis of the MIMIC-IV database.**

Authors: Jing L.;Shi X.;Xu L.;Zhao X.;Li F. and Qin, L.

Publication Date: 2025

Journal: Frontiers in Endocrinology 16(pagination), pp. Article Number: 1578078. Date of Publication: 2025

Abstract: Background: Sepsis remains a leading cause of mortality in intensive care units (ICUs), with high morbidity and healthcare costs worldwide. The serum anion gap (AG), a marker of metabolic acidosis, has been associated with adverse outcomes in various critical illnesses. However, the prognostic value of longitudinal AG trajectories in sepsis remains underexplored. This study explored the link between dynamic AG trajectories and all-cause mortality in critically ill septic patients. Method(s): A retrospective cohort study utilized data from the Medical Information Mart for Intensive Care IV (MIMIC-IV) database. Adult patients meeting Sepsis-3 criteria for sepsis were included. Group-based trajectory modeling was used to identify AG trajectories during the initial five days of ICU admission. Patients were classified into three trajectory groups: normal-level-stable trajectory (Class 1), high-level-decline trajectory (Class 2), and progressive acidosis trajectory (Class 3). Cox proportional hazards models evaluated the link between AG trajectories and ICU/hospital mortality, controlling for demographic, laboratory, and clinical severity factors. Subgroup and sensitivity analyses were performed to validate the findings. Result(s): Among 6,110 septic patients, three distinct AG trajectory groups were identified. Patients in Class 3 (decreasing high AG) had the highest mortality, with ICU mortality of 30.61% and hospital mortality of 35.85%, compared to Class 1 (ICU mortality: 14.46%, hospital mortality: 19.41%) and Class 2 (ICU mortality: 21.88%, hospital mortality: 31.88%). In fully adjusted models, Class 3 exhibited a significantly increased risk of ICU mortality [HR=1.72, (95% CI 1.43-2.07), PResult(s): Among 6,110 septic patients, three distinct AG trajectory groups were identified. Patients in Class 3 (decreasing high AG) had the highest mortality, with ICU mortality of 30.61% and hospital mortality of 35.85%, compared to Class 1 (ICU mortality: 14.46%, hospital mortality: 19.41%) and Class 2 (ICU mortality: 21.88%, hospital mortality: 31.88%). In fully adjusted models, Class 3 exhibited a significantly increased risk of ICU mortality [HR=1.72, (95% CI 1.43-2.07), PResult(s): Among 6,110 septic patients, three distinct AG trajectory groups were identified. Patients in Class 3 (decreasing high AG) had the highest mortality, with ICU mortality of 30.61% and hospital mortality of 35.85%, compared to Class 1 (ICU mortality: 14.46%, hospital mortality: 19.41%) and Class 2 (ICU mortality: 21.88%, hospital mortality: 31.88%). In fully adjusted models, Class 3 exhibited a significantly increased risk of ICU mortality [HR=1.72, (95% CI 1.43-2.07), PConclusion(s): Continuous monitoring of AG levels is crucial for risk assessment and personalized treatment, as rising AG levels significantly increase mortality risk. These findings underscore the potential of AG trajectories as a dynamic biomarker to improve sepsis management and patient outcomes.Copyright © 2025 Jing, Shi, Xu, Zhao, Li and Qin.

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7. **Sex Differences in Risk Factors for Incident Sepsis Hospitalizations: A Prospective Cohort Study Using the UK Biobank.**

Authors: Low G.K.K.;Harris K.;Woodward M. and Thompson, K. J.

Publication Date: 2025

Journal: Journal of Infectious Diseases 232(2), pp. 393–400

Abstract: Background Sepsis is a leading cause of death worldwide. The presence of most chronic conditions and other lifestyle-related risk factors increase sepsis risk. Whether there are sex differences in risk factors associated with sepsis hospitalization is unknown. Methods A prospective cohort study included participants aged 40-69 years recruited to the UK Biobank between 2006 and 2010. Sepsis was identified from hospitalization records. Poisson regression was used to estimate sex-specific incidence. Cox proportional hazards models were used to estimate hazard ratios (HRs) and the women-to-men ratio of HRs (RHR) with 95% confidence intervals (CIs) for risk factors associated with an incident sepsis hospitalization. Results Of 490 783 participants, 21 468 (47.6% women) experienced an incident sepsis hospitalization. Age-standardized risk was higher in men than in women (40.2 vs 31.2 per 10 000 person-years; HR, 1.26 [95% CI, 1.23-1.29]). Chronic obstructive pulmonary disease (COPD) conferred the highest risk for sepsis hospitalization, with excess risk in women (RHR, 1.23 [95% CI, 1.10-1.38]). Dyslipidemia (RHR, 1.08 [95% CI, 1.02-1.16]), myocardial infarction (1.22 [1.05-1.41]), and smoking (1.19 [1.09-1.29]) were associated with excess risk of sepsis hospitalization in women, compared with men. Dementia was associated with more than twice the risk of sepsis hospitalization in men (HR, 2.21 [95% CI, 1.37-3.55]). Conclusions The risk of sepsis hospitalization was higher in the presence of most risk factors, with greater effects in women with a history of COPD, dyslipidemia, myocardial infarction, and smoking. Incorporating sex-specific risk factors in risk prediction modeling may facilitate targeted prevention efforts and support earlier recognition and treatment.

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8. **Quality of early sepsis diagnostics in German intensive care units-Results of a nationwide survey.**

Authors: Michel S.;Renckhoff K.;Espeter F.;Richter D.;Weigand M.A.;Schurholz T.;Brenner T. and Dubler, S.

Publication Date: 2025

Journal: Anaesthesiologie 74(8), pp. 489–499

Abstract: Background: The management of sepsis patients remains an ongoing challenge in intensive care medicine and leads to unacceptably high morbidity and mortality rates, even in medically highly developed countries. Objective(s): What is the state of the quality of early sepsis treatment on German intensive care units (ICUs)? Material(s) and Method(s): To assess the quality of early sepsis treatment, we conducted a nationwide internet-based survey among members of the German Interdisciplinary Association of Critical Care and Emergency Medicine (DIVI). Result(s): A total of 1935 intensive care physicians across Germany were surveyed of whom 459 experienced specialist physicans responded, including 38% chief physicians and 61% senior physicians. Overall, 66% of participants reported the use of screening tools for early sepsis detection, with the quick-sepsis organ failure assessment (qSOFA) being the most frequently used (71%). In 32.7% of the surveyed ICUs a microbiologist was available around the clock. Interdisciplinary rounds involving a microbiologist or a clinical pharmacologist took place in 55.5% and 52.5% of ICUs, respectively. Molecular diagnostic procedures (e.g., SeptiFast) for rapid pathogen identification were available in only 10.9% of the surveyed ICUs. Discussion(s): In summary, the use of the qSOFA score remains widespread despite deviating recommendations in current international guidelines. Additionally, interdisciplinary rounds involving microbiology or pharmacology were conducted in only half of the participating ICUs. Molecular biological diagnostic procedures are still not part of the diagnostic standard in most hospitals. Graphic abstract: (Figure presented.)

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9. **Association of Omega-3 Status With Long-Term Risk of Hospitalization for Sepsis.**

Authors: Narayan, Deo;Vlasschaert, Caitlyn;Day, Andrew G.;Norman, Patrick;Rauh, Michael J. and

Maslove, David M.

Publication Date: Apr 01 ,2025

Journal: Critical Care Medicine 53(4), pp. e763–e771

Abstract: OBJECTIVES: Sepsis is a life-threatening condition characterized by a dysregulated host response to infection. Despite decades of clinical trials, there are no specific treatments; care of the nearly 50 million annual cases worldwide is limited to antimicrobials and supportive measures. A primary prevention strategy may therefore be of value. We hypothesized that higher premorbid omega-3 fatty acid levels would be associated with a reduced incidence of sepsis. DESIGN: Population-based cohort study. SETTING: Retrospective data from the United Kingdom (U.K. Biobank). PATIENTS: Two hundred seventy-three thousand three hundred twenty-five participants from the U.K. Biobank. INTERVENTIONS: None. MEASUREMENTS AND MAIN RESULTS: Our exposure was baseline estimated omega-3 index (eO3I), modeled both categorically in quartiles, and continuously with restricted cubic splines. Our outcome measure was hospital admission with an International Classification of Diseases , 10th Edition code consistent with sepsis. The median (interquartile range) baseline eO3I was 6.0% (4.8-7.3%). Over a mean follow-up period of 13 years, 9241 participants experienced hospitalization with sepsis. In our adjusted model, compared with the lowest eO3I quartile, participants had lower risks of sepsis incidence in the second quartile (hazard ratio [HR], 0.88; 95% CI, 0.86-0.91; p : Our exposure was baseline estimated omega-3 index (eO3I), modeled both categorically in quartiles, and continuously with restricted cubic splines. Our outcome measure was hospital admission with an International Classification of Diseases , 10th Edition code consistent with sepsis. The median (interquartile range) baseline eO3I was 6.0% (4.8-7.3%). Over a mean follow-up period of 13 years, 9241 participants experienced hospitalization with sepsis. In our adjusted model, compared with the lowest eO3I quartile, participants had lower risks of sepsis incidence in the second quartile (hazard ratio [HR], 0.88; 95% CI, 0.86-0.91; p : Our exposure was baseline estimated omega-3 index (eO3I), modeled both categorically in quartiles, and continuously with restricted cubic splines. Our outcome measure was hospital admission with an International Classification of Diseases , 10th Edition code consistent with sepsis. The median (interquartile range) baseline eO3I was 6.0% (4.8-7.3%). Over a mean follow-up period of 13 years, 9241 participants experienced hospitalization with sepsis. In our adjusted model, compared with the lowest eO3I quartile, participants had lower risks of sepsis incidence in the second quartile (hazard ratio [HR], 0.88; 95% CI, 0.86-0.91; p : Our exposure was baseline estimated omega-3 index (eO3I), modeled both categorically in quartiles, and continuously with restricted cubic splines. Our outcome measure was hospital admission with an International Classification of Diseases , 10th Edition code consistent with sepsis. The median (interquartile range) baseline eO3I was 6.0% (4.8-7.3%). Over a mean follow-up period of 13 years, 9241 participants experienced hospitalization with sepsis. In our adjusted model, compared with the lowest eO3I quartile, participants had lower risks of sepsis incidence in the second quartile (hazard ratio [HR], 0.88; 95% CI, 0.86-0.91; p : Our exposure was baseline estimated omega-3 index (eO3I), modeled both categorically in quartiles, and continuously with restricted cubic splines. Our outcome measure was hospital admission with an International Classification of Diseases , 10th Edition code consistent with sepsis. The median (interquartile range) baseline eO3I was 6.0% (4.8-7.3%). Over a mean follow-up period of 13 years, 9241 participants experienced hospitalization with sepsis. In our adjusted model, compared with the lowest eO3I quartile, participants had lower risks of sepsis incidence in the second quartile (hazard ratio [HR], 0.88; 95% CI, 0.86-0.91; p CONCLUSIONS: In this population-based cohort study, baseline eO3I was inversely associated with subsequent sepsis incidence. Given that omega-3 levels can be increased with dietary supplementation, primary prevention should be explored to mitigate the burden of sepsis.

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10. **Pre-analytical delay of blood cultures which hinders the management of sepsis and fosters the emergence of antimicrobial resistance is an adverse effect of laboratory centralisation.**

Authors: Noone, M.

Publication Date: 2025

Journal: medRxiv (pagination), pp. Date of Publication: 11 Jun 2025

Abstract: Background The clinical diagnosis of sepsis is based on non-specific criteria and blood culture remains the gold standard confirmatory test. While early results are of wide clinical benefit delayed reports lead to prolonged anti-microbial therapy which fosters the emergence of antimicrobial resistance. Pre-analytical delay of a blood culture delays or decreases the chance of a positive report and a maximal four-hour delay between collection and incubation of the specimen is recommended by the United Kingdom Standards for Microbiology Investigations (UK SMI). This retrospective observational study documents compliance with this quality standard by National Health Service (NHS) hospitals across England. An appraisal is undertaken of the policies which governed laboratory centralisation and their impact on the microbiology service. Methods Freedom of Information (FOI) applications were submitted to 116 NHS Trusts in England requesting retrospective audit data showing compliance with the recommended pre-analytical standard for blood cultures. Information relating to the configuration of microbiology services and global laboratory costs were also requested. Results Reports were received from 89 Trusts (76.7%) comprising 146 acute hospitals. Only four hospitals (2.7%) showed full compliance with the four-hour pre-analytical standard. Service configurations varied widely. The anticipated savings resulting from centralisation have not been realised. Conclusions There was poor compliance with the quality standard for pre-analytical delay of blood cultures. Evidence is presented to show that the poor compliance rates reported are a result of the approach taken and the guiding policies applied when laboratory centralisation was imposed by NHS England. Reversal of these adverse effects will require mandatory implementation of UK SMIs and computing the cost of quality measures in the context of the overall health care benefit to the patient.

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11. **Utilizing a Nurse Discharge Navigator to Reduce Readmissions for Hospitalized Patients With Sepsis: A Quality Improvement Feasibility Study.**

Authors: Pruitt M.;Matusik A.;Patel N. and Kreider, K.

Publication Date: 2025

Journal: Professional Case Management (pagination), pp. Date of Publication: 23 Jul 2025

Abstract: PURPOSE/OBJECTIVES: The purpose of this project was to evaluate the impact of a nurse discharge navigator implementing an education and structured outpatient follow-up program on reducing 30-day readmissions for adult patients with sepsis. PRIMARY PRACTICE SETTING: This project was implemented at an 847-bed academic hospital in the southeastern United States. FINDINGS/CONCLUSIONS: Patient capture in the study was poor, driven by high rates of cancer diagnoses, comfort-directed care, and frequent discharges to postacute care. Readmission rates for patients receiving the full intervention (n = 16) were 25% (n = 4). Overall readmission rates for patients with sepsis in 2024 were 13.3% (n = 61). The outcomes of this project were influenced by the advanced comorbidities of the participants. IMPLICATIONS FOR CASE MANAGEMENT PRACTICE: Case management of patients with sepsis should be comprehensive. Caregivers should be involved early to initiate education on the disease process, have clear communication with the follow-up team, and involve close, structured follow-up that can be adapted to the postacute care setting. One promising area for improvement of this intervention would be the inclusion of a Hospital at Home program as a transition program to the transition clinic.

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12. **Early empirical antibiotherapy in patients attended for suspected sepsis in emergency departments: a systematic review.**

Authors: Rodriguez, Marcelo R.;Llopis Roca, Ferran;Rubio Diaz, Rafael;Garcia, Dario Eduardo and Julian-Jimenez, Agustin

Publication Date: Feb ,2025

Journal: Emergencias 37(1), pp. 44–55

Abstract: OBJECTIVE: Patients with suspected infections account for 15% to 35% of hospital emergency department (ED) caseloads in Spain and Latin America. The main objective of this systematic review was to compare evidence supporting the safety and efficacy of early (3 hours after triage) vs deferred ($ 3-6 hours) antibiotic therapy prescribed in EDs for adults with serious infections or sepsis. Efficacy and improved clinical course were defined by reduced progression to septic shock and short- and long-term mortality. METHODS: The review was guided by the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA). PubMed, the Web of Sciencie, EMBASE, Lilacs, Cochrane, Epistemonikos, Tripdatabase, and ClinicalTrials.gov were searched for the period from January 1, 2010, to December 31, 2023. No language restrictions were set. We used the following Medical English Subject Headings and strings: "Antibiotic OR Antibiotic Treatment OR Antibiotic Therapy OR Early Antibiotic Treatment OR Early Antibiotic Therapy," "Infection OR Bacterial Infection OR Sepsis," "Emergencies OR Emergency OR Emergency Department," "Timing," "Early," and "Adults." Observational cohort studies were included. To evaluate quality of research design and risk of bias, we applied the Newcastle-Ottawa Scale. Case-control studies, narrative reviews and other types of articles were excluded. We completed a narrative review of the findings and did not undertake meta-analysis. The review was registered in the PROSPERO database (CRD42024520687). RESULTS: The search yielded 1528 articles, of which 7 met the criteria for inclusion and analysis. The 7 studies comprised data for 118349 patients, 74141 of whom (62.6%) received early antibiotic treatment. Three studies were classified as high quality, 3 moderate, and 1 low. The 3 high-quality studies provided information on 2 aspects: 1) hospital and short-term mortality and 2) long-term mortality. One high-quality study showed a tendency for hospital and 30-day mortality to increase when antibiotics were administered more than 6 hours after triage vs within 1 hour of triage (hazard ratio, 2.25; 95% CI, 0.91-5.59; P = .08). Another reported an adjusted odds ratio of 1.09 (95% CI, 1.05-1.13; P = .024) for hospital mortality associated with each hour of therapeutic delay after triage. The third study reported that each additional hour of delay after triage was associated with a 10% increase (95% CI, 5%-14%; P .001) in the probability of 360-day mortality. Finally, the single low-quality study reported that each hour of delay in treatment was associated with an odds ratio of 1.08 (95% CI, 1.02-1.04; P .001) for increased risk of septic shock. CONCLUSIONS: Early initiation of antibiotic therapy, preferably within 3 hours of triage, can be recommended in cases of serious infection (sepsis or serious sepsis that do not meet the criteria for septic shock). In fact, based on a tendency for higher short- and long-term mortality associated with delay and a higher probability of developing septic shock with each hour of delay, therapy should start as soon as possible if infection is confirmed or suspected in the absence of an alternative diagnosis.; Publisher OBJETIVO: La atencion de pacientes con sospecha de un proceso infeccioso en los servicios de urgencias hospitalarios (SUH) supone el 15%-35% de todas las atenciones en Espana y Latinoamerica. Esta revision sistematica (RS) compara si la administracion precoz de la antibioterapia (en 3 horas desde que el paciente se recibe en el triaje) en pacientes adultos atendidos en los SUH por infeccion grave o sepsis, en comparacion con la administracion diferida (> 3-6 horas), es mas eficaz y segura y mejora la evolucion clinica al disminuir la progresion a shock septico (SS) y la mortalidad a corto y largo plazo. METODO: Se realiza una RS siguiendo la normativa PRISMA en las bases de datos de PubMed, Web of Sciencie, EMBASE, Lilacs, Cochrane, Epistemonikos, Tripdatabase y ClinicalTrials.gov desde desde 1 de enero de 2010 hasta el 31 de diciembre de 2023 sin restriccion de idiomas y utilizando una combinacion de terminos MESH: "Antibiotic OR Antibiotic Treatment OR Antibiotic Therapy OR Early Antibiotic Treatment OR Early Antibiotic Therapy", "Infection OR Bacterial Infection OR Sepsis", "Emergencies OR Emergency OR Emergency Department", "Timing", "Early" y "Adults". Se incluyeron estudios de cohortes observacionales. Para valorar la calidad del metodo empleado y el riesgo de sesgos de los articulos incluidos se utilizo la Newcastle-Ottawa Scale (NOS). No se incluyeron estudios de casos y controles, revisiones narrativas y otros tipos de articulos. No se realizaron tecnicas de metanalisis, pero los resultados se compararon narrativamente. El protocolo de la RS se registro en PROSPERO (CRD42024520687). RESULTADOS: Se identificaron 1.528 articulos de los cuales se analizaron finalmente 7, que incluyen 118.349 pacientes, 74.141 de ellos (62,6%) con administracion precoz de antibiotico (AB). Tres estudios fueron calificados de calidad alta, 3 moderada y 1 baja. En relacion a los resultados de los estudios de calidad alta se encontro lo siguiente: 1) con la mortalidad hospitalaria

y a corto plazo (30 dias) en funcion del tiempo de administracion del AB desde el triaje y la gravedad de la sepsis: el primer estudio de calidad alta publica una tendencia a aumentar la mortalidad cuando se administro el AB en > 6 horas desde el triaje en comparacion con administracion en 1 hora (HR = 2,25; IC 95%: 0,91-5,59; p = 0,08); el segundo muestra una OR ajustada para mortalidad hospitalaria por cada hora de tiempo de administracion del AB desde el triaje de 1,09 (IC 95%: 1,05-1,13; p = 0,024); 2) con la mortalidad a largo plazo el tercer estudio muestra como cada hora adicional hasta el inicio del AB se asocia con un aumento del 10% (IC 95%: 5-14; p 0,001) de probabilidad de morir a los 360 dias. Finalmente, un estudio de calidad baja muestra como el tiempo (en horas) hasta la primera administracion del AB obtiene una OR de 1,03 (IC 95%: 1,02-1,04; p 0,001) para la progresion al SS. CONCLUSIONES: En los casos de infeccion grave (sepsis o sepsis grave) sin cumplir criterios de SS, se puede recomendar la administracion precoz de la terapia antimicrobiana preferiblemente en las tres primeras horas (en realidad lo antes posible, en cuanto se pueda confirmar o se mantenga la sospecha sin encontrar otro diagnostico distinto), ya que se ha confirmado la tendencia a aumentar la mortalidad a corto y a largo plazo y una mayor probabilidad de evolucionar a SS cuando se demora la administracion del AB cada hora. Language: Spanis

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13. **Diagnostic and Prognostic Utility of Inflammatory Biomarkers in Sepsis-Associated Acute Kidney Injury: A Case-Control Study.**

Authors: Sadana S.;Kumar D.;Ahuja K.;Malik D.;Mumtaz A.;Srivastava S. and Khan, S.

Publication Date: 2025

Journal: International Journal of Life Sciences Biotechnology and Pharma Research 14(7), pp. 1538–1546

Abstract: Introduction: Sepsis is a life-threatening condition characterized by a dysregulated host response to infection, frequently leading to organ dysfunction such as acute kidney injury (AKI). Early identification of sepsis-associated AKI (S-AKI) is critical to improving patient outcomes. This study aimed to evaluate the predictive and prognostic utility of inflammatory biomarkers-interleukin-6 (IL-6), C-reactive protein (CRP), tumor necrosis factor-alpha (TNF-alpha), and E-selectin-in patients with sepsis, with and without AKI, and to determine their association with morbidity and mortality. Material(s) and Method(s): A case-control study was conducted over 24 months at Era's Lucknow Medical College & Hospital, including adult sepsis patients divided into two groups: those with AKI (cases) and those without AKI (controls). Biomarkers were assessed via serum levels, and statistical analyses included multivariate t-tests and Receiver Operating Characteristic (ROC) curves to evaluate diagnostic accuracy. Morbidity and mortality were analyzed in relation to biomarker levels. Result(s): IL-6 was significantly elevated in the AKI group (137.34 +/- 55.34 pg/mL) compared to controls (59.77 +/- 53.19 pg/mL, pResult(s): IL-6 was significantly elevated in the AKI group (137.34 +/- 55.34 pg/mL) compared to controls (59.77 +/- 53.19 pg/mL, pConclusion(s): IL-6 emerged as the most reliable inflammatory biomarker for early detection of AKI and prediction of mortality and morbidity in sepsis. CRP demonstrated supportive value, while TNF-alpha and E-selectin had limited prognostic relevance. These findings suggest incorporating IL-6 in sepsis management protocols could enhance early risk stratification and improve clinical outcomes.

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14. **Heterogeneity in association of myocardial injury and mortality in sepsis or acute respiratory distress syndrome by subphenotype: a retrospective study.**

Authors: Sanchez P.A.;Obeidalla S.;Kerchberger V.E.;Moore A.R.;Maddali M.V.;Kangelaris K.N.;Hendrickson C.M.;Evrard B.;Liu K.D.;Bastarache J.A.;Matthay M.A.;Rogers A.J. and Calfee, C. S.

Publication Date: 2025

Journal: Critical Care 29(1) (pagination), pp. Article Number: 363. Date of Publication: 01 Dec 2025

Abstract: Rationale: Myocardial injury is common in acute respiratory distress syndrome (ARDS) and sepsis and associated with increased mortality. Two latent class analysis derived subphenotypes are

associated with differential risk of mortality in these populations, though the association of troponin-I with mortality within each subphenotype is unknown. Method(s): The derivation (n = 597 in EARLI) and validation (n = 452 in VALID) cohorts consisted of patients with sepsis or ARDS admitted to the ICU and enrolled in two separate prospective observational studies. Patients with troponin-I measured between hospital presentation and within 24 h of ICU admission were included. A parsimonious classifier model using interleukin-8, soluble tumor necrosis factor receptor-1, and vasopressor use assigned patients to subphenotype. Association between peak troponin-I concentration and 60-day in-hospital mortality within each subphenotype was assessed through logistic regression adjusting for age, admission laboratory values, vasopressor use, invasive ventilation use, and cardiac comorbidities. Result(s): Median peak troponin-I was significantly higher in the hyperinflammatory vs hypoinflammatory subphenotype in both cohorts (0.07 vs 0.04 ng/mL and 0.17 vs 0.07 ng/mL, both p Result(s): Median peak troponin-I was significantly higher in the hyperinflammatory vs hypoinflammatory subphenotype in both cohorts (0.07 vs 0.04 ng/mL and 0.17 vs 0.07 ng/mL, both p Conclusion(s): Admission peak troponin-I is significantly associated with 60-day mortality in patients with sepsis or ARDS. This association was distinctly driven by the hypoinflammatory subphenotype.

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15. **Nonlinear Association Between Calculated Globulin Levels and 28-Day Mortality in Patients with Sepsis: A Retrospective Cohort Study.**

Authors: She X.;Zhao X.;Yang H. and Cui, X.

Publication Date: 2025

Journal: Risk Management and Healthcare Policy 18, pp. 2743–2757

Abstract: Background: Sepsis remains a significant global health challenge, causing approximately 11 million deaths annually. The calculated globulin (CG) level, which is derived from total protein and albumin levels, plays crucial roles in the immune response and inflammation. However, the relationship between the CG level and sepsis mortality remains unexplored. Method(s): This retrospective cohort study analyzed sepsis patients from the eICU Collaborative Research Database. The primary outcome was 28-day ICU mortality. The relationship between the CG level and mortality was examined via generalized additive models with penalized splines and two piecewise linear regression models. Confounders were adjusted in multivariate analyzes. Result(s): The overall 28-day ICU mortality was 10.0% among 9110 sepsis patients (mean age 65.3 +/- 15.9 years, 48.7% male). An L-shaped relationship was observed between CG level and mortality, with a threshold of 2.9 g/dL (95% CI: 2.8-2.9). This pattern revealed that mortality risk decreased sharply as globulin levels increased to 2.9 g/dL and then plateaued thereafter. Below this threshold, each 1 g/dL increase in the CG was associated with a significantly reduced mortality risk (adjusted OR = 0.51, 95% CI: 0.40-0.64, P Result(s): The overall 28-day ICU mortality was 10.0% among 9110 sepsis patients (mean age 65.3 +/- 15.9 years, 48.7% male). An L-shaped relationship was observed between CG level and mortality, with a threshold of 2.9 g/dL (95% CI: 2.8-2.9). This pattern revealed that mortality risk decreased sharply as globulin levels increased to 2.9 g/dL and then plateaued thereafter. Below this threshold, each 1 g/dL increase in the CG was associated with a significantly reduced mortality risk (adjusted OR = 0.51, 95% CI: 0.40-0.64, P Conclusion(s): This study revealed an L-shaped relationship between CG level and sepsis mortality, with lower CG levels independently associated with increased mortality risk. This finding provides a simple and cost-effective indicator for risk stratification in sepsis patients, facilitating early identification of high-risk individuals and informing clinical decision-making.

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16. **Association Between Malnutrition and Sepsis-Associated Delirium: A Retrospective Analysis of the MIMIC-IV Database.**

Authors: Tan W.;Duan R.;Zeng C.;Yang Z.;Dai L.;Xu T.;Zhu L. and Sun, D.

Publication Date: 2025

Journal: Nursing in Critical Care 30(5), pp. e70130

Abstract: BACKGROUND: In individuals with sepsis, the most frequent neurological consequence is sepsis-associated delirium (SAD). SAD can cause long-term neuropsychiatric aftereffects such as anxiety disorders and cognitive impairment in addition to dramatically raising death rates in the intensive care unit (ICU) and during hospital stays. However, the correlation between nutritional status and SAD in patients with sepsis remains undefined. AIM: To examine the correlation between malnutrition and the incidence of SAD in sepsis patients. STUDY DESIGN: This research performed a retrospective analysis of adult patients with sepsis who were admitted to the ICU for the initial time. It investigated the association between malnutrition and delirium using logistic regression analysis. It employed propensity score matching, conducted stratified analysis and utilised E-value for sensitivity analysis. RESULT(S): This study included 25 716 patients, of whom 3132 were classified as malnourished and 22 584 were non-malnourished. The malnourished cohort demonstrated a twofold increased risk of delirium relative to the non-malnourished cohort (26.56% vs. 12.90%). Multifactorial logistic regression demonstrated a significant positive correlation between malnutrition and the occurrence of delirium in sepsis patients within a fully adjusted model (odds ratio [OR] = 2.07, 95% confidence interval [CI] = 1.88-2.29). The findings remained consistent following a series of sensitivity analyses. CONCLUSION(S): Malnutrition is strongly correlated with the occurrence of delirium in patients with sepsis. The significance of addressing malnutrition in sepsis patients within the ICU warrants attention. RELEVANCE TO CLINICAL PRACTICE: ICU nurses should prioritise the assessment of malnutrition, particularly among patients with sepsis. Timely identification and nutritional intervention in these patients may reduce care costs and lower the risk of delirium.

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17. **Impact of early beta-blocker use on the incidence of sepsis and clinical outcomes following cardiac surgery: a retrospective cohort study.**

Authors: Yin C.;Guan C.;Ma Q.;Zhang S.;Chen Q. and Xiao, B.

Publication Date: 2025

Journal: Frontiers in Pharmacology 16(pagination), pp. Article Number: 1615868. Date of Publication: 2025

Abstract: Background: Sepsis after cardiac surgery represents a severe perioperative complication with high incidence and mortality rates. While the cardioprotective benefits of beta-blocker following cardiac surgery are widely recognized, their impact on sepsis development remains unclear. This study aims to investigate the association between early postoperative beta-blocker use and the incidence of sepsis, as well as clinical outcomes, in patients undergoing cardiac surgery. Method(s): The analysis incorporated data from the MIMIC-IV database, with confounding factors addressed through propensity score matching (PSM), inverse probability of treatment weighting (IPTW), and overlap weighting (OW). Logistic regression models assessed the risk of sepsis and in-hospital mortality, while Cox proportional hazards models evaluated 28-day and 1-year mortality. Kaplan-Meier survival curves and log-rank tests compared survival between groups. Sensitivity analyses using Fine-Gray competing risk models and cumulative incidence functions were performed. Subgroup analyses explored heterogeneity of treatment effects, and metoprolol was further stratified by dose to assess dose-response relationships. Result(s): A total of 3,154 patients treated with beta-blocker and 5,220 controls were included. Early beta-blocker use was associated with a reduced risk of sepsis and lower in-hospital mortality across all methods. For 28-day and 1-year mortality, beta-blocker use showed a trend toward risk reduction. Competing risk analyses demonstrated lower cumulative incidence of sepsis in the beta-blocker group. Subgroup and dose-response analyses indicated that both low and high doses of metoprolol were associated with reduced postoperative sepsis risk and mortality outcomes. Conclusion(s): Early use of beta-blocker after cardiac surgery was associated with a lower incidence of sepsis, with potential benefits observed in both short-term and long-term prognosis. These findings provide valuable evidence for optimizing perioperative drug management strategies.

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18. **Pancreatic enzyme replacement therapy can improve infection level nutrition condition and**

prognosis of patients with sepsis.

Authors: Zhao L. and Wang, S.

Publication Date: 2025

Journal: Food and Nutrition Research 69(pagination), pp. Article Number: 12746. Date of Publication: 2025

Abstract: Objective: This study aimed to investigate the effects of pancreatic enzyme replacement therapy (PERT) on infection level, nutrition condition and prognosis of patients with sepsis. Method(s): According to the fecal elastase-1 (FE1) level, 68 sepsis patients who were diagnosed with pancreatic exocrine insufficiency (PEI) from 2014.11 to 2015. 12 in our hospital were randomly divided into two groups: regular nutritional support (RNS) group or PERT group. A total of 15 patients were dropout for various reasons. Finally, 25 patients were enrolled in PERT group and 28 in RNS group. APACHEII score, SOFA score, inflammatory biomarkers including C-reaction protein (CRP), white blood cell (WBC), procalcitonin (PCT), nutrition markers including prealbumin (PA), transferrin (TFN), retinol binding protein (RBP), creatinine/ height index (CHI) were recorded at the day 1 (D1), day7 (D7) and day14 (D14) since they were admitted in ICU. These data were compared between and within the two groups chronologically. Also, the duration of vasoactive drug using (DVAD), mechanical ventilation (DMV), length of stay in ICU (LOS) and survival rate within 14 days were compared between the two groups. Result(s): There were no differences in general information (Age and gender) between PERT and RNS groups. Compared with the RNS group, CRP, WBC and PCT declined significantly at D14 in the PERT group. Especially, CRP declined significantly over time in both groups. In addition, compared with the RNS group, in the PERT group at D14, nutrition markers, including PA, TFN, RBP and CHI increased significantly, APACHEII score and SOFA score decreased significantly. And DVAD, DMV and LOS were significantly shortened in PERT group, but the survival rate within 14 days was not significantly changed. Conclusion(s): The PERT can improve infection level, nutrition condition and prognosis of patients with sepsis. And the underlying mechanism may be related to improve pancreatic exocrine insufficiency of these patients.

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19. **Impact of serum calcium levels on the occurrence of sepsis and prognosis in hospitalized patients with concomitant psoriasis: a retrospective study based on the MIMIC-IV database.**

Authors: Zheng X.;Su Q.;Wang Y. and Geng, X.

Publication Date: 2025

Journal: Frontiers in Immunology 16(pagination), pp. Article Number: 1621231. Date of Publication: 2025

Abstract: Objective: This study aims to investigate the relationship between serum calcium levels during hospitalization and the incidence and prognosis of sepsis in hospitalized patients with psoriasis. Method(s): A retrospective analysis of patients with concomitant psoriasis admitted for the first time was conducted, utilizing the Medical Information Mart for Intensive Care database. Machine learning techniques, along with logistic regression, Cox regression, group-based trajectory modeling (GBTM), and mediation analysis, were employed to assess the influence of serum calcium levels and other clinical indicators on the occurrence of sepsis and all-cause mortality. Result(s): Serum calcium exhibits a significant inverse correlation with the occurrence of sepsis [odds ratio (OR) =0.351, 95% CI: 0.265-0.463, PResult(s): Serum calcium exhibits a significant inverse correlation with the occurrence of sepsis [odds ratio (OR) =0.351, 95% CI: 0.265-0.463, PResult(s): Serum calcium exhibits a significant inverse correlation with the occurrence of sepsis [odds ratio (OR) =0.351, 95% CI: 0.265-0.463, PResult(s): Serum calcium exhibits a significant inverse correlation with the occurrence of sepsis [odds ratio (OR) =0.351, 95% CI: 0.265-0.463, PConclusion(s): Serum calcium levels serve as a significant predictive factor for the occurrence and prognosis of sepsis in hospitalized patients with psoriasis. Continuous monitoring of serum calcium levels and timely correction of hypocalcemia may contribute positively to improving patient outcomes.

Sources Used:

The following databases are used in the creation of this bulletin: EMBASE and Medline.

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