



# Predicting critical care outcomes in acute respiratory infections: The interplay between host comorbidities and immune status

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## ABSTRACT

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Acute respiratory infections (ARIs) are a major cause of global critical illness and remain a leading reason for intensive care unit (ICU) admission and mortality. While pathogen-related factors and treatment timing have long dominated prognostic research, recent evidence highlights the decisive influence of host characteristics, particularly comorbidities and immune competence, on clinical outcomes. Chronic diseases such as diabetes, cardiovascular disorders, chronic kidney or liver disease, and chronic obstructive pulmonary disease substantially modify the course of ARIs by amplifying systemic inflammation, altering immune regulation, and impairing pulmonary and multi-organ recovery. Similarly, primary and secondary immunosuppression arising from malignancy, transplantation, or therapeutic interventions further increase the risk of severe infection, ventilator dependency, and mortality. Despite these associations, current prognostic models in respiratory critical care largely depend on physiologic or pathogen-specific variables, overlooking the complex host interplay that determines disease severity and treatment response. This narrative review synthesizes contemporary evidence on how comorbidities and immune alterations shape outcomes in critically ill patients with ARIs, with a focus on mortality, duration of mechanical ventilation, and ICU length of stay. It addresses key research questions regarding the relative contribution of host versus pathogen factors, the prognostic value of immune-inflammatory biomarkers, and the potential integration of host data into predictive models. Understanding this interplay is essential for advancing precision critical care, guiding individualized management, and informing the development of ethical, host-inclusive frameworks for ICU triage and resource allocation in increasingly multimorbid populations.

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## 1. Introduction

Acute respiratory infections (ARIs) remain among the leading causes of morbidity and mortality worldwide, with a particularly high impact on intensive care unit (ICU) populations [1]. Recent epidemiological data indicate that ARIs account for millions of hospitalizations each year and impose a substantial burden on healthcare resources [1]. Outcomes among critically ill patients vary substantially across studies and regions, with significant differences observed in mortality rates, duration of mechanical ventilation, and ICU length of stay [2]. For example, a multicenter study of ICU patients with viral respiratory infections reported an all-cause mortality rate of approximately 30% [3]. While pathogen virulence and treatment timing play central roles, host factors including comorbidities and immune competence are increasingly recognized as critical determinants of prognosis [4-6]. Chronic diseases such as diabetes mellitus, chronic obstructive pulmonary disease (COPD), cardiovascular disease, and chronic kidney disease (CKD) are frequently associated with higher ICU mortality and prolonged mechanical ventilation in ARI patients [7]. Data from the LUNG SAFE study demonstrated that ICU mortality rose from 27% among patients with no comorbidity to 46% in those with immune incompetence and 67% in patients with chronic liver failure [4].

Moreover, immunosuppression whether due to cancer therapy, organ transplantation, or systemic corticosteroid therapy has been consistently associated with higher susceptibility to severe acute respiratory infections, prolonged ICU stays, and increased mortality [8,9]. Despite these findings, prognostic models in respiratory critical care remain focused mainly on physiological indices (e.g., PaO<sub>2</sub>/FiO<sub>2</sub> ratio, sequential organ failure assessment [SOFA]) or pathogen-specific variables rather than host determinants. Given the high prevalence of multimorbidity and immunosenescence in ICU populations, understanding the interplay between comorbidities and immune dysfunction is crucial to refining risk stratification and improving outcomes [10-13].

Therefore, this narrative review aims to synthesize recent evidence on how pre-existing comorbidities and immune alterations influence outcomes mortality, length of stay, and ventilator dependency in critically ill patients with acute respiratory infections.

## 2. Epidemiological overview of ARIs in ICU

Globally, ARIs remain a leading cause of ICU admissions for respiratory failure [1]. In a ten-year European study, ICU admissions for ARIs increased among older adults, with mortality rates reaching approximately 20% in patients aged 75-89 years [14]. Data from multiple regions confirm that the burden of ARIs in ICUs is driven by both bacterial (e.g., *Streptococcus pneumoniae*, *Klebsiella pneumoniae*) and viral pathogens, including influenza, respiratory

syncytial virus (RSV), and SARS-CoV-2 [15-18]. Recent multicenter studies have quantified this burden: in one large cohort, the incidence of viral respiratory infections in the ICU was 30.45 per 10,000 patient-days, with a mortality rate of 22.1% [2]. In a retrospective cohort of 807 ICU patients with severe respiratory infections due to four viruses (RSV, SARS-CoV-2, seasonal influenza, H1N1), patients in the RSV group had a significantly greater comorbidity burden compared with the other groups, and outcome variation was observed across pathogens [3].

The overlap between chronic disease prevalence and ARI outcomes is particularly notable. For instance, in a Swiss cohort of adults hospitalized with RSV, 98% had at least one comorbidity, and both CKD (OR 2.64) and immunosuppression (OR 5.7) were independently associated with severe disease and ICU admission [19]. Comparable findings have been observed in coronavirus disease 2019 (COVID-19) cohorts, where immunocompromised status predicted longer ventilation and higher mortality [20].

ICU resource utilization in ARI is significant. Studies report that a significant proportion of patients require respiratory support, including invasive or non-invasive mechanical ventilation, along with continuous hemodynamic and monitoring support throughout their ICU stay [21]. Beyond acute mortality, ARI survivors often experience post-ICU sequelae, including reduced pulmonary function and increased readmission risk [22].

Together, these findings highlight that while pathogens and treatment strategies contribute to ICU outcomes, regional comorbidity profiles and immune competence substantially modify risk. The heterogeneity of outcomes underscores the importance of integrating host factors into predictive models and critical care protocols for ARIs.

## 3. Comorbidities as predictors of ICU outcomes

Comorbidities play a pivotal role in shaping outcomes among critically ill patients with ARIs. Beyond pathogen virulence, the host's baseline health status including cardiometabolic, respiratory, renal, and hepatic diseases strongly influences mortality, ventilation requirements, and ICU length of stay [23-25]. Recent studies emphasize that multimorbidity and frailty contribute to worse recovery outcomes and higher post-ICU complications, underscoring the need for individualized prognostic assessment and tailored management in this heterogeneous population [26].

### 3.1 Cardiometabolic comorbidities

Patients with cardiometabolic disorders particularly diabetes mellitus and obesity represent a high-risk subgroup among those admitted to the ICU for ARIs. Diabetes, obesity and overweight are associated with impaired immune regulation and increased systemic

inflammation, which together contribute to higher disease severity and mortality in patients with ARIs such as COVID-19 [27]. In a retrospective study of 650 hospitalized COVID-19 patients, those with diabetes had significantly higher rates of ICU admission (35.4% vs 27.7%;  $p = 0.035$ ) and need for invasive ventilation (17.5% vs 11.4%;  $p = 0.026$ ) compared with non-diabetics [28]. Obesity adds further complexity to respiratory critical illness. Excess adiposity influences ventilatory mechanics by increasing chest wall and abdominal pressures, reducing lung compliance and contributing to ventilation–perfusion mismatch. A recent analysis of 19,311 ICU patients found that patients with higher BMI had a greater likelihood of receiving mechanical ventilation, although obesity appeared paradoxically associated with lower mortality in some cohorts [29]. These findings underscore that while obesity may predispose to respiratory deterioration in ARI, its relationship with ICU outcome is multifactorial and may reflect a complex interplay of physiology, inflammatory status and treatment response.

### 3.2 Chronic respiratory and cardiovascular diseases

Pre-existing respiratory diseases such as COPD, asthma and interstitial lung disease diminish baseline pulmonary reserve and contribute to worse clinical outcomes [30]. In a recent retrospective study of 100 ICU-admitted COPD patients, 43% required invasive mechanical ventilation, and the ICU and 90-day mortality rates were 21% and 39%, respectively [13]. These findings highlight that impaired pulmonary mechanics and systemic inflammation in COPD amplify the severity of respiratory infections and worsen critical care outcome [13]. Co-existing cardiac dysfunction significantly increases the risk of adverse outcomes in critically ill patients with ARIs, as heart failure leads to combined pulmonary–vascular compromise that prolongs ventilator dependence, promotes multi-organ dysfunction, and raises ICU mortality; for instance, previous multicenter studies reported that patients with pre-existing heart failure had nearly double the ICU mortality rate compared with those without cardiac disease [31,32].

### 3.3 Chronic kidney and liver diseases

Chronic kidney disease (CKD) and chronic liver disease (CLD) both alter immune homeostasis and pharmacokinetics of ICU therapies. Patients with CKD exhibit impaired clearance of inflammatory mediators and antimicrobials, increasing vulnerability to infection and treatment failure. One large-scale observational study found that, among diabetic patients with ARIs, CKD significantly increased the odds of ICU admission ( $OR \approx 1.88$ ) and invasive ventilation ( $OR \approx 2.16$ ) [28]. In CLD, portal hypertension and hepatic immunodeficiency may amplify systemic inflammatory

response, delay resolution of infection and prolong ICU stay. Although direct ICU ARI-specific data remain limited, the cumulative evidence suggests these organ failures markedly increase host vulnerability [33,34]. As a result, liver dysfunction in critically ill patients not only exacerbates systemic and pulmonary inflammatory responses but also increases the risk of developing acute respiratory distress syndrome (ARDS). This dysfunction impairs bacterial clearance and detoxification of harmful mediators, aggravating lung injury and contributing to worsened outcomes in patients with liver disease [35]. Although this is a bidirectional relationship, as has been recently shown in critically ill patients with liver cirrhosis, the development of ARDS within the first 72 hours of ICU admission significantly increases 28-day and 90-day mortality rates, highlighting its role as a major prognostic factor for poor outcomes [36].

### 3.4 Multimorbidity and frailty

Multimorbidity defined as the presence of  $\geq 2$  chronic conditions and frailty reflect a host phenotype of diminished physiologic reserve and increased vulnerability in the critical care setting [37]. Traditional prognostic models often undervalue this “host vulnerability”. Evidence consistently indicates that ICU patients with ARIs tend to be older and have a heavier burden of chronic diseases compared with non-ARDS or general populations [38]. Frail patients are more likely to require prolonged mechanical ventilation, experience ICU-acquired complications (e.g., delirium, neuromuscular blockade), and have longer ICU and hospital lengths of stay. Recognizing multimorbidity in ARI patients may improve risk stratification and help select personalized management pathways [1,39,40].

## 4. Immune status and immunosuppression in ICU infections

Immune competence is a decisive determinant of prognosis in critically ill patients with ARIs. Both innate and adaptive immune functions can be profoundly altered by pre-existing conditions or therapeutic immunosuppression, leading to higher infection risk and poorer clinical outcomes. Recent ICU studies highlight that immune dysregulation whether due to hematologic malignancies, corticosteroid exposure, or biologic therapies modifies disease severity, ventilator dependence, and mortality rates, emphasizing the importance of incorporating immune-status assessment into critical-care decision-making [41–43].

### 4.1 Primary versus secondary immunosuppression

Immunological impairment in ICU patients admitted with ARIs can stem from primary (inborn) immune defects or more commonly from acquired (secondary) immunosuppression [44,45]. While congenital immune

deficiency remains rare in adult critical-care populations, secondary immunosuppression arises from conditions such as HIV infection, hematologic malignancies, organ transplantation, chemotherapy, high-dose corticosteroids or biologic therapies [44,45]. Outcomes in ICU patients with ARIs and immunosuppression are heterogeneous. In the landmark multicenter study by Azoulay et al., which included 1,004 cancer patients with ARDS across 14 ICUs, 86% had hematologic malignancies and 44% presented with neutropenia; nearly 90% of ARDS cases were infection-related, one-third due to invasive fungal infections, and overall hospital mortality reached 64% [41].

Also, a recent post-hoc analysis further confirmed that, beyond in-ICU mortality, immunocompromised survivors remain at substantial long-term risk, where among 299 patients, 6-month mortality approached 50%, with solid cancers and higher SOFA scores being independent predictors of poor outcome [43]. Together, these findings highlight that acquired immunosuppression not only increases vulnerability to infection-related ARDS but also shapes ICU management decisions and post-discharge trajectories, complicating critical-care recovery.

#### 4.2 Mechanisms of immune impairment

The pathophysiology of immunosuppression in ARI-related ICU admissions involves multiple mechanisms including lymphocyte exhaustion, cytokine imbalance, and dysregulated neutrophil activity [46]. In a recent cohort study of immunocompromised ICU patients, authors observed profound lymphopenia, elevated neutrophil counts, and high neutrophil/lymphocyte ratios (NLR), indicating suppressed adaptive immunity and exaggerated innate inflammation [47].

These alterations impair pathogen clearance and predispose patients to secondary infections and worsening pulmonary injury. For example, in the global LUNG SAFE study encompassing 2,813 patients with ARDS from 459 ICUs, 20.8% were immunocompromised, most commonly due to pneumonia or non-pulmonary sepsis; their hospital mortality (52.4%) was significantly higher than that of immunocompetent patients (36.2%) despite comparable ARDS severity highlighting how immune dysfunction worsens outcome [43].

#### 4.3 COVID-19 as a model

The COVID-19 pandemic provided a unique model to study the effects of immune status on ICU outcomes. Patients receiving immunosuppressive therapies exhibited T-cell dysfunction, altered cytokine profiles, and diminished viral clearance, which contributed to worse outcomes in many reports.

Investigations of immunocompromised COVID-19 ICU cohorts revealed that pre-existing immunosuppression was associated with increased ventilatory requirements and multi-organ failure,

though some studies noted no significant difference in mortality when early aggressive ICU management was employed [48,49].

These observations underscore the need for refined prognostic frameworks that integrate immune-status parameters to optimize treatment in ARI-critical-care settings.

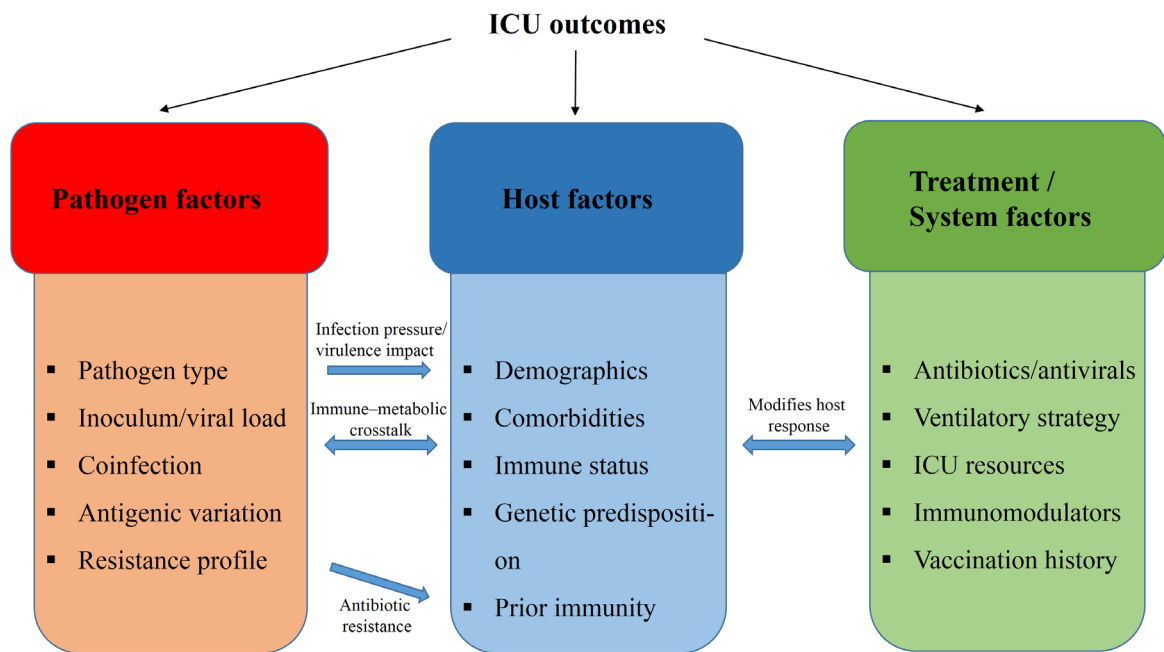
### 5. Integrating host factors into prognostic models

Traditionally employed ICU prognostic scoring systems such as the acute physiology and chronic health evaluation (APACHE II) and SOFA scores provide valuable mortality risk estimates in general critical-care populations, but they lack detailed incorporation of host immune status or specific comorbidity burden [50,51]. For example, although the SOFA score correlates with mortality in sepsis, its incremental prognostic value beyond age, comorbidity and infection severity is modest [50,51].

Thus, current models may not fully capture the heterogeneity observed in patients with ARIs who present with varied host factors. Emerging research has therefore explored integrating genetic, immunologic and detailed comorbidity data into precision prognostic frameworks.

A recent systematic review of AI/ML prognostic models for in-hospital mortality in intensive care analysed 15 retrospective studies (2015–2025) and found that, although machine-learning approaches (notably XGBoost, random forest and various neural-network architectures) generally outperformed conventional scores such as APACHE, SOFA and SAPS, the reviewed models largely relied on routinely collected physiologic and laboratory variables from a small set of retrospective databases (principally MIMIC and eICU-CRD) and rarely incorporated dedicated immune-inflammatory biomarkers or genomic features. The review therefore concludes that current ICU prognostic models do not yet integrate host immune-status data in a systematic or standardized way, and it highlights methodological weaknesses (retrospective design, limited external validation, heterogeneity in preprocessing and performance reporting) that must be addressed before immune-biomarker-driven ML models can be widely adopted in clinical practice [52].

Biomarkers such as C-reactive protein (CRP), interleukin-6 (IL-6) and Nod-like receptors NLRs have been shown to improve prediction of in predicting the severity or outcomes in patients with COVID-19 [4]. Also, elevated IL-6 and NLR on admission in COVID-19 patients with diabetes predicted need for ICU care [53]. Figure 1 illustrates the layered conceptual framework proposed in this review, highlighting how pathogen factors, host comorbidities, and immune competence interact with therapeutic modifiers to determine ICU outcomes in patients with acute respiratory infections.



**Figure 1.** Interactions between host, pathogen, and ICU outcomes in ARIs. This schematic illustrates the multifactorial interactions determining outcomes (ICU mortality, ventilator days, length of stay, and readmission) in ARIs requiring intensive care. Pathogen-related factors (such as virulence variation, load, and resistance) interact with host determinants including comorbidities, age, and baseline immune competence to influence disease severity and clinical trajectory. Treatment-related variables, such as timing of antimicrobial therapy, ventilatory strategy, and resource availability, further modify these relationships. Immune status functions (e.g. CRP, IL-6, NLR, lymphocyte count, HLA profile, serostatus) as a central mediator linking host vulnerability to infection outcomes, modulating the inflammatory response, organ dysfunction, and recovery potential. Understanding this dynamic interplay supports personalized risk assessment and precision-guided critical care for patients with severe respiratory infections.)

## 6. Clinical implications

The complex interaction between host comorbidities and immune status in ARIs has direct implications for critical-care practice. Personalized risk stratification is essential for optimizing management in the ICU, allowing clinicians to shape respiratory support, antimicrobial therapy, and immunomodulatory interventions to individual patient profiles. Integrating host-specific factors such as metabolic disease, immune suppression, and chronic organ dysfunction into early triage can refine prognosis and guide intensity of monitoring [54-58].

Preventive strategies are pivotal, as optimizing the management of chronic conditions such as diabetes and cardiovascular disease, together with prioritizing vaccination against respiratory pathogens like influenza and pneumococcus, may reduce the likelihood of ICU admission and lead to improved downstream clinical outcomes [59,60].

Multicenter prospective studies combining host phenotyping, immune profiling, and genomic data are needed to establish predictive biomarkers and guide precision-based therapies [61,62].

At a systems level, ethical considerations remain central to ICU triage and resource allocation, particularly for immunocompromised or multimorbid patients who face heightened vulnerability. Developing

equitable, evidence-based frameworks that incorporate host risk factors into admission and treatment decisions is therefore critical for advancing precision and fairness in critical-care medicine.

## 7. Conclusion

Host-related factors particularly comorbidities and immune competence are decisive determinants of outcomes in patients with acute respiratory infections admitted to intensive care. Evidence from recent multicentre studies indicates that the interaction between metabolic, cardiorespiratory, renal, and hepatic dysfunctions, together with acquired or treatment-related immunosuppression, substantially influences mortality, mechanical-ventilation duration, and recovery trajectories. Despite advances in infection management, current prognostic tools remain limited by their insufficient integration of host biology. Incorporating immune-inflammatory biomarkers, genomic signatures, and detailed comorbidity indices into predictive models could enhance precision in risk stratification and treatment planning. Future research should prioritize prospective, multicentric validation of such models and establish ethical, evidence-based frameworks to ensure equitable allocation of critical-care resources in increasingly multimorbid ICU populations.

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During the preparation of this manuscript, AI-assisted tools were used solely for language refinement and improving the clarity of the text. All generated or edited content was carefully reviewed, verified, and approved by the authors to ensure accuracy and integrity.

## Authors' contributions

NK, OKM: conceptualized and defined the scope of the review. NK: conducted the literature search and organized the data. OKM: prepared the initial draft of the manuscript. NK, OKM: provided critical revision and intellectual input to refine the manuscript. All authors read and approved the final version of article.

## Conflict of interest

No potential conflict of interest was reported by the authors.

## Ethical declarations

Not applicable.

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## References

- Cui C, Timbrook TT, Polacek C, Heins Z, Rosenthal NA. Disease burden and high-risk populations for complications in patients with acute respiratory infections: a scoping review. *Front Med (Lausanne)*. 2024;11:1325236. DOI: [10.3389/fmed.2024.1325236](https://doi.org/10.3389/fmed.2024.1325236) PMID: [38818396](https://pubmed.ncbi.nlm.nih.gov/38818396/)
- Kim JY, Yang KS, Chung Y, Lee KB, Suh JW, Kim SB, et al. Epidemiologic Characteristics and Clinical Significance of Respiratory Viral Infections Among Adult Patients Admitted to the Intensive Care Unit. *Front Med (Lausanne)*. 2022;9:829624. DOI: [10.3389/fmed.2022.829624](https://doi.org/10.3389/fmed.2022.829624) PMID: [35685411](https://pubmed.ncbi.nlm.nih.gov/35685411/)
- Grangier B, Vacheron CH, De Marignan D, Casalegno JS, Couray-Targe S, Bestion A, et al. Comparison of mortality and outcomes of four respiratory viruses in the intensive care unit: a multicenter retrospective study. *Sci Rep*. 2024;14(1):6690. DOI: [10.1038/s41598-024-55378-x](https://doi.org/10.1038/s41598-024-55378-x) PMID: [38509095](https://pubmed.ncbi.nlm.nih.gov/38509095/)
- Rezoagli E, McNicholas BA, Madotto F, Pham T, Bellani G, Laffey JG, et al. Presence of comorbidities alters management and worsens outcome of patients with acute respiratory distress syndrome: insights from the LUNG SAFE study. *Ann Intensive Care*. 2022;12(1):42. DOI: [10.1186/s13613-022-01015-7](https://doi.org/10.1186/s13613-022-01015-7) PMID: [35596885](https://pubmed.ncbi.nlm.nih.gov/35596885/)
- Xu Y, Qi L, Yang J, Duan Y, Jiang M, Sun Y, et al. Factors affecting the severity of respiratory infections: a hospital-based cross-sectional study. *BMC Infect Dis*. 2025;25(1):735. DOI: [10.1186/s12879-025-11121-z](https://doi.org/10.1186/s12879-025-11121-z) PMID: [40410688](https://pubmed.ncbi.nlm.nih.gov/40410688/)
- Dumas G, Bertrand M, Lemiale V, Canet E, Barbier F, Kouatchet A, et al. Prognosis of critically ill immunocompromised patients with virus-detected acute respiratory failure. *Ann Intensive Care*. 2023;13(1):101. DOI: [10.1186/s13613-023-01196-9](https://doi.org/10.1186/s13613-023-01196-9) PMID: [37833435](https://pubmed.ncbi.nlm.nih.gov/37833435/)
- Quarg C, Jörres RA, Engelhardt S, Alter P, Budweiser S. Characteristics and outcomes of patients hospitalized for infection with influenza, SARS-CoV-2 or respiratory syncytial virus in the season 2022/2023 in a large German primary care centre. *Eur J Med Res*. 2023;28(1):568. DOI: [10.1186/s40001-023-01482-z](https://doi.org/10.1186/s40001-023-01482-z) PMID: [38053110](https://pubmed.ncbi.nlm.nih.gov/38053110/)
- Vena A, Giacobbe DR, Di Biagio A, Mikulska M, Taramasso L, De Maria A, et al. Clinical characteristics, management and in-hospital mortality of patients with coronavirus disease 2019 in Genoa, Italy. *Clin Microbiol Infect*. 2020;26(11):1537-1544. DOI: [10.1016/j.cmi.2020.07.049](https://doi.org/10.1016/j.cmi.2020.07.049) PMID: [32810610](https://pubmed.ncbi.nlm.nih.gov/32810610/)
- Li C, He H, Wang Y, Huang L, Chen Z, Zhang Q, et al. Outcomes and inflammation changes in different types of immunocompromised patients with critically ill COVID-19 admitted to ICU: a national multicenter study. *BMC Pulm Med*. 2024;24(1):548. DOI: [10.1186/s12890-024-03362-6](https://doi.org/10.1186/s12890-024-03362-6) PMID: [39482633](https://pubmed.ncbi.nlm.nih.gov/39482633/)
- Gutierrez-Zamudio AAM, Alejandro-Salinas R, Vereau-Robles JI, Toro-Huamanchumo CJ. Prognostic performance of the Age, PaO<sub>2</sub>/FiO<sub>2</sub> Ratio, and Plateau Pressure Score (APPS) for mortality in patients with COVID-19-associated acute respiratory distress syndrome admitted to an intensive care unit. *Ther Adv Infect Dis*. 2024;11:20499361241306212. DOI: [10.1177/20499361241306212](https://doi.org/10.1177/20499361241306212) PMID: [39678996](https://pubmed.ncbi.nlm.nih.gov/39678996/)
- Jeong D, Lee GT, Park JE, Hwang SY, Kim T, Lee SU, et al. Prognostic Accuracy of SpO<sub>2</sub>-based Respiratory Sequential Organ Failure Assessment for Predicting In-hospital Mortality. *West J Emerg Med*. 2023;24(6):1056-1063. DOI: [10.5811/westjem.59417](https://doi.org/10.5811/westjem.59417) PMID: [38165187](https://pubmed.ncbi.nlm.nih.gov/38165187/)
- Chowdhury SR, Chandra Das D, Sunna TC, Beyene J, Hossain A. Global and regional prevalence of multimorbidity in the adult population in community settings: a systematic review and meta-analysis. *EClinicalMedicine*. 2023;57:101860. DOI: [10.1016/j.eclinm.2023.101860](https://doi.org/10.1016/j.eclinm.2023.101860) PMID: [36864977](https://pubmed.ncbi.nlm.nih.gov/36864977/)
- Akbaş T, Güneş H. Characteristics and outcomes of patients with chronic obstructive pulmonary disease admitted to the intensive care unit due to acute hypercapnic respiratory failure. *Acute Crit Care*. 2023;38(1):49-56. DOI: [10.4266/acc.2022.01011](https://doi.org/10.4266/acc.2022.01011) PMID: [36935534](https://pubmed.ncbi.nlm.nih.gov/36935534/)
- Laporte L, Hermetet C, Jouan Y, Gaborit C, Rouve E, Shea KM, et al. Ten-year trends in intensive care admissions for respiratory infections in the elderly. *Ann Intensive Care*. 2018;8(1):84. DOI: [10.1186/s13613-018-0430-6](https://doi.org/10.1186/s13613-018-0430-6) PMID: [30112650](https://pubmed.ncbi.nlm.nih.gov/30112650/)
- Seo YB, Song JY, Choi MJ, Kim IS, Yang TU, Hong KW, et al. Etiology and clinical outcomes of acute respiratory virus infection in hospitalized adults. *Infect Chemother*. 2014;46(2):67-76. DOI: [10.3947/ic.2014.46.2.67](https://doi.org/10.3947/ic.2014.46.2.67) PMID: [25024868](https://pubmed.ncbi.nlm.nih.gov/25024868/)
- Demboux Lyelet JE, Mayengue PI, Koukouikila-Koussounda F, Leroy EM, Becquart P, Niama FR. Viral and Bacterial Etiology of Common Respiratory Infections in Children in Sub-Saharan Africa: A Systematic Review. *Children (Basel)*. 2025;12(9):1212. DOI: [10.3390/children12091212](https://doi.org/10.3390/children12091212) PMID: [41007077](https://pubmed.ncbi.nlm.nih.gov/41007077/)
- Siddik AB, Tanvir NA, Bhuyan GS, Alam MS, Islam Z, Bulbul MRH, et al. Bacterial and viral etiology of acute respiratory infection among the Forcibly Displaced Myanmar Nationals (FDMNs) in fragile settings in Cox's Bazar- a prospective case-control study. *PLoS Negl Trop Dis*. 2023;17(4):e0011189. DOI: [10.1371/journal.pntd.0011189](https://doi.org/10.1371/journal.pntd.0011189) PMID: [37036845](https://pubmed.ncbi.nlm.nih.gov/37036845/)
- Xu M, He W, Xie S, Ren Z, Chen J, Nuerbolati B. Epidemiological and pathological characterization of acute respiratory infections. *APMIS*. 2025;133(1):e13484. DOI: [10.1111/apm.13484](https://doi.org/10.1111/apm.13484) PMID: [39444293](https://pubmed.ncbi.nlm.nih.gov/39444293/)
- Joseph N, Passavant EDB, Lüthi-Corridori G, Jaun F, Mitrovic S, Leuppi JD, et al. Association of Comorbidities with Adverse Outcomes in Adults Hospitalized with Respiratory Syncytial Virus (RSV) Infection: A Retrospective Cohort Study from Switzerland (2022-2024). *Viruses*. 2025;17(8):1030. DOI: [10.3390/v17081030](https://doi.org/10.3390/v17081030) PMID: [40872745](https://pubmed.ncbi.nlm.nih.gov/40872745/)

20. Duo X, Deshpande K. Characteristics and Outcomes of Immunocompromised Patients With COVID-19 Infection Admitted to an Intensive Care Unit: A Retrospective Cohort Study. *Cureus*. 2025;17(9):e92961. DOI: [10.7759/cureus.92961](https://doi.org/10.7759/cureus.92961) PMID: [41133078](https://pubmed.ncbi.nlm.nih.gov/41133078/)
21. Martin-Loeches I, Reyes LF, Nseir S, Ranzani O, Povoia P, Diaz E, et al. European Network for ICU-Related Respiratory Infections (ENIRRI): a multinational, prospective, cohort study of nosocomial LRTI. *Intensive Care Med*. 2023;49(10):1212-1222. DOI: [10.1007/s00134-023-07210-9](https://doi.org/10.1007/s00134-023-07210-9) PMID: [37812242](https://pubmed.ncbi.nlm.nih.gov/37812242/)
22. Colbenson GA, Johnson A, Wilson ME. Post-intensive care syndrome: impact, prevention, and management. *Breathe (Sheff)*. 2019;15(2):98-101. DOI: [10.1183/20734735.0013-2019](https://doi.org/10.1183/20734735.0013-2019) PMID: [31191717](https://pubmed.ncbi.nlm.nih.gov/31191717/)
23. Lee KS, Park DI, Lee J, Oh O, Kim N, Nam G. Relationship between comorbidity and health outcomes in patients with heart failure: a systematic review and meta-analysis. *BMC Cardiovasc Disord*. 2023;23(1):498. DOI: [10.1186/s12872-023-03527-x](https://doi.org/10.1186/s12872-023-03527-x) PMID: [37817062](https://pubmed.ncbi.nlm.nih.gov/37817062/)
24. Khan Chachar AZ, Asif M, Tanveer K, Rauf MK, Iqbal J, Khan K, et al. Clinical Characteristics, Comorbidities, and Outcome of Critically Sick Patients With COVID-19 Pneumonia Admitted in the Intensive Care Unit of a Tertiary Care Hospital in Lahore, Pakistan: A Retrospective Cohort Study. *Cureus*. 2022;14(5):e25286. DOI: [10.7759/cureus.25286](https://doi.org/10.7759/cureus.25286) PMID: [35755515](https://pubmed.ncbi.nlm.nih.gov/35755515/)
25. Kreutmair S, Kauffmann M, Unger S, Ingelfinger F, Núñez NG, Alberti C, et al. Preexisting comorbidities shape the immune response associated with severe COVID-19. *J Allergy Clin Immunol*. 2022;150(2):312-324. DOI: [10.1016/j.jaci.2022.05.019](https://doi.org/10.1016/j.jaci.2022.05.019) PMID: [35716951](https://pubmed.ncbi.nlm.nih.gov/35716951/)
26. Stewart J, Bradley J, Smith S, McPeake J, Walsh T, Haines K, et al. Do critical illness survivors with multimorbidity need a different model of care? *Crit Care*. 2023;27(1):485. DOI: [10.1186/s13054-023-04770-6](https://doi.org/10.1186/s13054-023-04770-6) PMID: [38066562](https://pubmed.ncbi.nlm.nih.gov/38066562/)
27. Nagy É, Cseh V, Barcs I, Ludwig E. The Impact of Comorbidities and Obesity on the Severity and Outcome of COVID-19 in Hospitalized Patients-A Retrospective Study in a Hungarian Hospital. *Int J Environ Res Public Health*. 2023;20(2):1372. DOI: [10.3390/ijerph20021372](https://doi.org/10.3390/ijerph20021372) PMID: [36674133](https://pubmed.ncbi.nlm.nih.gov/36674133/)
28. Zakerkish M, Fooladi MS, Shahbazian HB, Ahmadi F, Peyman Payami S, Dargahi-Malamir M. Assessment of Mortality Rate, Need for ICU Admission and Ventilation in COVID-19 Patients with Diabetes Mellitus. *Qatar Med J*. 2022;2022(1):9. DOI: [10.5339/qmj.2022.9](https://doi.org/10.5339/qmj.2022.9) PMID: [35291286](https://pubmed.ncbi.nlm.nih.gov/35291286/)
29. Yu W, Jiang W, Yuan J, Fan T, Xiao H, Sun L, et al. Association between BMI and outcomes in critically ill patients: an analysis of the MIMIC-III database. *Sci Rep*. 2024;14(1):31127. DOI: [10.1038/s41598-024-82424-5](https://doi.org/10.1038/s41598-024-82424-5) PMID: [39730662](https://pubmed.ncbi.nlm.nih.gov/39730662/)
30. Han MK, Criner GJ, Halpin DMG, Kerwin EM, Tombs L, Lipson DA, et al. Any Decrease in Lung Function is Associated With Worse Clinical Outcomes: Post Hoc Analysis of the IMPACT Interventional Trial. *Chronic Obstr Pulm Dis*. 2024;11(1):106-113. DOI: [10.15326/jcopdf.2023.0391](https://doi.org/10.15326/jcopdf.2023.0391) PMID: [38081161](https://pubmed.ncbi.nlm.nih.gov/38081161/)
31. Zapata L, Guía C, Gómez R, García-Paredes T, Colinas L, Portugal-Rodríguez E, et al. Clinical presentation and outcomes of acute heart failure in the critically ill patient: A prospective, observational, multicentre study. *Med Intensiva (Engl Ed)*. 2023;47(4):221-231. DOI: [10.1016/j.medine.2022.03.001](https://doi.org/10.1016/j.medine.2022.03.001) PMID: [36272910](https://pubmed.ncbi.nlm.nih.gov/36272910/)
32. Li G, Cook DJ, Thabane L, Friedrich JO, Crozier TM, Muscedere J, et al. Risk factors for mortality in patients admitted to intensive care units with pneumonia. *Respir Res*. 2016;17(1):128. DOI: [10.1186/s12931-016-0444-2](https://doi.org/10.1186/s12931-016-0444-2) PMID: [27401184](https://pubmed.ncbi.nlm.nih.gov/27401184/)
33. Mannion R, Fitzpatrick E. Systemic Complications Secondary to Chronic Liver Disease. *Indian J Pediatr*. 2024;91(3):286-293. DOI: [10.1007/s12098-023-04694-7](https://doi.org/10.1007/s12098-023-04694-7) PMID: [37440151](https://pubmed.ncbi.nlm.nih.gov/37440151/)
34. McGettigan B, Hernandez-Tejero M, Malhi H, Shah V. Immune Dysfunction and Infection Risk in Advanced Liver Disease. *Gastroenterology*. 2025;168(6):1085-1100. DOI: [10.1053/j.gastro.2024.08.046](https://doi.org/10.1053/j.gastro.2024.08.046) PMID: [39927926](https://pubmed.ncbi.nlm.nih.gov/39927926/)
35. Herrero R, Sánchez G, Asensio I, López E, Ferruelo A, Vaquero J, et al. Liver-lung interactions in acute respiratory distress syndrome. *Intensive Care Med Exp*. 2020;8(Suppl 1):48. DOI: [10.1186/s40635-020-00337-9](https://doi.org/10.1186/s40635-020-00337-9) PMID: [33336286](https://pubmed.ncbi.nlm.nih.gov/33336286/)
36. Tariparast PA, Roedel K, Horvatits T, Drolz A, Kluge S, Fuhrmann V. Impact of acute respiratory distress syndrome on outcome in critically ill patients with liver cirrhosis. *Sci Rep*. 2025;15(1):4301. DOI: [10.1038/s41598-025-88606-z](https://doi.org/10.1038/s41598-025-88606-z) PMID: [39905232](https://pubmed.ncbi.nlm.nih.gov/39905232/)
37. Skou ST, Mair FS, Fortin M, Guthrie B, Nunes BP, Miranda JJ, et al. Multimorbidity. *Nat Rev Dis Primers*. 2022;8(1):48. DOI: [10.1038/s41572-022-00376-4](https://doi.org/10.1038/s41572-022-00376-4) PMID: [35835758](https://pubmed.ncbi.nlm.nih.gov/35835758/)
38. Aronsson Dannewitz A, Svenblad B, Michaëlsson K, Lipsey M, Gedeberg R. The long-term conditional mortality rate in older ICU patients compared to the general population. *Crit Care*. 2024;28(1):368. DOI: [10.1186/s13054-024-05147-z](https://doi.org/10.1186/s13054-024-05147-z) PMID: [39543756](https://pubmed.ncbi.nlm.nih.gov/39543756/)
39. Rashid M, Ramakrishnan M, Muthu DS, Chandran VP, Thunga G, Kunhikatta V, et al. Factors affecting the outcomes in patients with acute respiratory distress syndrome in a tertiary care setting. *Clin Epidemiol Glob Health*. 2022;13:100972. DOI: [10.1016/j.cegh.2022.100972](https://doi.org/10.1016/j.cegh.2022.100972) PMID: [37309426](https://pubmed.ncbi.nlm.nih.gov/37309426/)
40. Ahlström B, Frithiof R, Larsson IM, Strandberg G, Lipsey M, Hultström M. A comparison of impact of comorbidities and demographics on 60-day mortality in ICU patients with COVID-19, sepsis and acute respiratory distress syndrome. *Sci Rep*. 2022;12(1):15703. DOI: [10.1038/s41598-022-19539-0](https://doi.org/10.1038/s41598-022-19539-0) PMID: [36127433](https://pubmed.ncbi.nlm.nih.gov/36127433/)
41. Azoulay E, Lemiale V, Mokart D, Pène F, Kouatchet A, Perez P, et al. Acute respiratory distress syndrome in patients with malignancies. *Intensive Care Med*. 2014;40(8):1106-14. DOI: [10.1007/s00134-014-3354-0](https://doi.org/10.1007/s00134-014-3354-0) PMID: [24898895](https://pubmed.ncbi.nlm.nih.gov/24898895/)
42. Métails M, Frat JP, Ehrmann S, Pène F, Decavèle M, Terzi N, et al. Factors associated with ICU mortality and long-term outcomes in immunocompromised patients admitted to the intensive care unit for acute respiratory failure. *Ann Intensive Care*. 2025;15(1):175. DOI: [10.1186/s13613-025-01578-1](https://doi.org/10.1186/s13613-025-01578-1) PMID: [41168567](https://pubmed.ncbi.nlm.nih.gov/41168567/)
43. Cortegiani A, Madotto F, Gregoretti C, Bellani G, Laffey JG, Pham T, et al. Immunocompromised patients with acute respiratory distress syndrome: secondary analysis of the LUNG SAFE database. *Crit Care*. 2018;22(1):157. DOI: [10.1186/s13054-018-2079-9](https://doi.org/10.1186/s13054-018-2079-9) PMID: [29895331](https://pubmed.ncbi.nlm.nih.gov/29895331/)
44. Kim VHD, Upton JEM, Derfalvi B, Hildebrand KJ, McCusker C. Inborn errors of immunity (primary immunodeficiencies). *Allergy Asthma Clin Immunol*. 2025;20(Suppl 3):76. DOI: [10.1186/s13223-024-00938-z](https://doi.org/10.1186/s13223-024-00938-z) PMID: [39780212](https://pubmed.ncbi.nlm.nih.gov/39780212/)
45. Tuano KS, Seth N, Chinen J. Secondary immunodeficiencies: An overview. *Ann Allergy Asthma Immunol*. 2021;127(6):617-626. DOI: [10.1016/j.anai.2021.08.413](https://doi.org/10.1016/j.anai.2021.08.413) PMID: [34481993](https://pubmed.ncbi.nlm.nih.gov/34481993/)
46. Tirelli C, De Amici M, Albrici C, Mira S, Nalesso G, Re B, et al. Exploring the Role of Immune System and Inflammatory Cytokines in SARS-CoV-2 Induced Lung Disease: A Narrative Review. *Biology (Basel)*. 2023;12(2):177. DOI: [10.3390/biology12020177](https://doi.org/10.3390/biology12020177) PMID: [36829456](https://pubmed.ncbi.nlm.nih.gov/36829456/)
47. Chen X, Zhu X, Zhuo H, Lin J, Lin X. Basophils absence predicts poor prognosis and indicates immunosuppression of patients in intensive care units. *Sci Rep*. 2023;13(1):18533. DOI: [10.1038/s41598-023-45865-y](https://doi.org/10.1038/s41598-023-45865-y) PMID: [37898659](https://pubmed.ncbi.nlm.nih.gov/37898659/)
48. Guggilla V, Pacheco JA, Carvalho AM, Whitmer GR, Pawlowski AE, Johnson JL, et al. Immunosuppression variably impacts outcomes for patients hospitalized with COVID-19: A retrospective cohort study. *PLoS One*. 2025;20(8):e0330110. DOI: [10.1371/journal.pone.0330110](https://doi.org/10.1371/journal.pone.0330110) PMID: [40779550](https://pubmed.ncbi.nlm.nih.gov/40779550/)

49. Belsky JA, Tullius BP, Lamb MG, Sayegh R, Stanek JR, Auletta JJ. COVID-19 in immunocompromised patients: A systematic review of cancer, hematopoietic cell and solid organ transplant patients. *J Infect.* 2021;82(3):329-338. DOI: [10.1016/j.jinf.2021.01.022](https://doi.org/10.1016/j.jinf.2021.01.022) PMID: [33549624](https://pubmed.ncbi.nlm.nih.gov/33549624/)
50. Innocenti F, Tozzi C, Donnini C, De Villa E, Conti A, Zanobetti M, et al. SOFA score in septic patients: incremental prognostic value over age, comorbidities, and parameters of sepsis severity. *Intern Emerg Med.* 2018;13(3):405-412. DOI: [10.1007/s11739-017-1629-5](https://doi.org/10.1007/s11739-017-1629-5) PMID: [28188577](https://pubmed.ncbi.nlm.nih.gov/28188577/)
51. Safarnezhad Tameshkel F, Mandehgar-Najafabadi M, Ahmadzadeh M, Anoushirvani A, Alibeik N, Dini P, et al. Evaluation of three common scoring systems in COVID-19 patients: neutrophil-lymphocyte ratio (NLR), The Acute Physiology and Chronic Health Evaluation II (APACHE II), and C-reactive protein (CRP). *Ann Med Surg (Lond).* 2023;86(2):811-818. DOI: [10.1097/MS9.0000000000001503](https://doi.org/10.1097/MS9.0000000000001503) PMID: [38333304](https://pubmed.ncbi.nlm.nih.gov/38333304/)
52. Dhami A, Onyeukwu KA, Sattar S, Batra A, Mostafa Y, Haris M, et al. The Prognostic Performance of Artificial Intelligence and Machine Learning Models for Mortality Prediction in Intensive Care Units: A Systematic Review. *Cureus.* 2025;17(8):e90465. DOI: [10.7759/cureus.90465](https://doi.org/10.7759/cureus.90465) PMID: [40978923](https://pubmed.ncbi.nlm.nih.gov/40978923/)
53. Făgărășan I, Rusu A, Comșa H, Simu TD, Vultur DM, Todea DA. IL-6 and Neutrophil/Lymphocyte Ratio as Markers of ICU Admittance in SARS-CoV-2 Patients with Diabetes. *Int J Mol Sci.* 2023;24(19):14908. DOI: [10.3390/ijms241914908](https://doi.org/10.3390/ijms241914908) PMID: [37834356](https://pubmed.ncbi.nlm.nih.gov/37834356/)
54. Lagina M, Valley TS. Diagnosis and Management of Acute Respiratory Failure. *Crit Care Clin.* 2024;40(2):235-253. DOI: [10.1016/j.ccc.2024.01.002](https://doi.org/10.1016/j.ccc.2024.01.002) PMID: [38432694](https://pubmed.ncbi.nlm.nih.gov/38432694/)
55. Shen J, Yan J, Xie J, Li L. Proposing a novel ABCDEF framework for managing critical illness in geriatrics: challenges and perspectives. *Ann Med.* 2025;57(1):2579797. DOI: [10.1080/07853890.2025.2579797](https://doi.org/10.1080/07853890.2025.2579797) PMID: [41157965](https://pubmed.ncbi.nlm.nih.gov/41157965/)
56. Marini JJ. Evolving concepts in the ventilatory management of acute respiratory distress syndrome. *Clin Chest Med.* 1996;17(3):555-75. DOI: [10.1016/s0272-5231\(05\)70331-2](https://doi.org/10.1016/s0272-5231(05)70331-2) PMID: [8875011](https://pubmed.ncbi.nlm.nih.gov/8875011/)
57. Yang W, Li Z, Yang T, Li Y, Xie Z, Feng L, et al. Experts' Consensus on the Management of Respiratory Disease Syndemic. *China CDC Wkly.* 2024;6(8):131-138. DOI: [10.46234/ccdcw2024.029](https://doi.org/10.46234/ccdcw2024.029) PMID: [38476822](https://pubmed.ncbi.nlm.nih.gov/38476822/)
58. Phua J, Weng L, Ling L, Egi M, Lim CM, Divatia JV, et al. Intensive care management of coronavirus disease 2019 (COVID-19): challenges and recommendations. *Lancet Respir Med.* 2020;8(5):e42. DOI: [10.1016/S2213-2600\(20\)30186-7](https://doi.org/10.1016/S2213-2600(20)30186-7) PMID: [32272080](https://pubmed.ncbi.nlm.nih.gov/32272080/)
59. Micheletto C, Aliberti S, Andreoni M, Blasi F, Di Marco F, Di Matteo R, et al. Vaccination Strategies in Respiratory Diseases: Recommendation from AIPO-ITS/ETS, SIMIT, SIP/IRS, and SItI. *Respiration.* 2025;104(8):556-574. DOI: [10.1159/000544919](https://doi.org/10.1159/000544919) PMID: [40058339](https://pubmed.ncbi.nlm.nih.gov/40058339/)
60. Lian R, Zhang H, An Y, Chen Z. Chronic Diseases and Influenza Vaccines. *Vaccines (Basel).* 2025;13(9):936. DOI: [10.3390/vaccines13090936](https://doi.org/10.3390/vaccines13090936) PMID: [41012139](https://pubmed.ncbi.nlm.nih.gov/41012139/)
61. Davoudi F, Moradi A, Becker TM, Lock JG, Abbey B, Fontanarosa D, et al. Genomic and Phenotypic Biomarkers for Precision Medicine Guidance in Advanced Prostate Cancer. *Curr Treat Options Oncol.* 2023;24(10):1451-1471. DOI: [10.1007/s11864-023-01121-z](https://doi.org/10.1007/s11864-023-01121-z) PMID: [37561382](https://pubmed.ncbi.nlm.nih.gov/37561382/)
62. Georgakopoulou VE, Lempesis IG, Sklapani P, Trakas N, Spandidos DA. Precision medicine for respiratory diseases: A current viewpoint. *Med Int (Lond).* 2024;4(4):31. DOI: [10.3892/mi.2024.155](https://doi.org/10.3892/mi.2024.155) PMID: [38680944](https://pubmed.ncbi.nlm.nih.gov/38680944/)