Saudi Journal of Medicine and Public Health

https://saudijmph.com/index.php/pub

https://doi.org/10.64483/202522349

Complications of Mechanical Ventilation: Nursing Assessment and Management

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Abstract

Background: Mechanical ventilation is a life-saving intervention for critically ill patients but is associated with significant complications, including ventilator-associated events (VAEs), ventilator-induced lung injury (VILI), and ventilator-associated pneumonia (VAP). These complications increase morbidity, mortality, and healthcare costs.

Aim: To review the complications of mechanical ventilation and outline nursing assessment and management strategies to mitigate these risks.

Methods: This narrative review synthesizes evidence from CDC surveillance frameworks, epidemiologic studies, and clinical guidelines, focusing on pathophysiology, risk factors, and preventive strategies for VAEs, VILI, and VAP.

Results: VAEs occur in 5–6% of ventilated patients, with infection-related complications and VAP contributing to prolonged ICU stays and higher mortality. VILI mechanisms include atelectrauma, barotrauma, volutrauma, and biotrauma, while VAP remains a major infectious complication, often caused by multidrug-resistant organisms. Preventive strategies include lung-protective ventilation (low tidal volume, optimal PEEP), prone positioning, ECMO in severe cases, and ventilator bundles incorporating head-of-bed elevation, oral care, and sedation management. Nursing plays a pivotal role in implementing these interventions, monitoring for early deterioration, and ensuring multidisciplinary coordination.

Conclusion: Mechanical ventilation, while essential, carries substantial risk. Evidence-based preventive strategies and vigilant nursing care are critical to reducing complications and improving outcomes.

Keywords: Mechanical ventilation, ventilator-associated events, ventilator-induced lung injury, ventilator-associated pneumonia, nursing management, critical care.

Introduction

Mechanical ventilation remains a cornerstone of life-sustaining therapy for patients experiencing critical illness, providing vital support when spontaneous ventilation is inadequate. Despite its indispensable role in modern intensive care, this intervention is inherently associated with a spectrum of clinically important complications, many of which are considered avoidable through timely recognition and evidence-informed practice. These adverse events extend beyond mechanical or technical issues and include serious pulmonary and systemic sequelae such as ventilator-associated pneumonia (VAP), sepsis, acute respiratory distress syndrome (ARDS), atelectasis, and pulmonary edema.[1] The occurrence of ventilator-associated complications is strongly associated with worsened patient trajectories and constitutes a major contributor to preventable harm in high-acuity settings. Such complications frequently amplify morbidity and may increase mortality risk, particularly among physiologically vulnerable populations requiring prolonged ventilatory support. Moreover, these events can delay liberation from mechanical ventilation, extend hospitalization, and lengthen time spent in the intensive care unit (ICU), thereby placing additional burdens on health systems

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Receive Date: 25 November 2025, Revise Date: 20 December 2025, Accept Date: 22 December 2025

and escalating overall health care expenditures.[2] Consequently, the development and implementation of safe, effective preventive and therapeutic approaches are not optional adjuncts but essential elements of high-quality critical care. Achieving meaningful risk reduction typically depends on coordinated multidisciplinary engagement, integrating clinical expertise from nursing, respiratory therapy, medicine, and infection prevention. This collaborative framework is central to optimizing patient safety and limiting adverse outcomes linked to ventilator-associated events (VAEs).

Function Surveillance

The Centers for Disease Control and Prevention (CDC) introduced an updated surveillance framework for ventilator-associated events (VAEs) in 2013 in response to recognized shortcomings in earlier surveillance approaches, particularly those published in 2005. The central motivation for this revision was the pursuit of greater objectivity and reproducibility in identifying ventilator-associated complications across diverse intensive care settings. Earlier parameters for ventilator-associated pneumonia (VAP), while clinically meaningful, were frequently criticized for their reliance on subjective clinical interpretation, variability in radiographic assessment, and inconsistent application between institutions. By contrast, the 2013 framework sought to standardize surveillance by emphasizing more quantifiable respiratory deterioration patterns and clearly defined thresholds. Importantly, this framework was designed primarily to support epidemiologic monitoring, benchmarking, and quality improvement initiatives rather than to serve as a bedside diagnostic tool guiding direct clinical management. Accordingly, numerous advantages and limitations have been described in relation to its implementation and its relationship to clinical outcomes.[3] A principal strength of the CDC's 2013 VAE model lies in its greater parameter objectivity. The surveillance definitions emphasize measurable changes in ventilator settings, such as worsening oxygenation requirements, which can be consistently captured and interpreted across institutions. This emphasis is intended to reduce interobserver variability and enhance the reliability of reported event rates, thereby improving comparisons between units, hospitals, and health systems. A related advantage is the practical feasibility of electronic computation. Because the surveillance criteria are anchored in discrete, routinely recorded ventilator variables, they lend themselves to automated extraction from electronic health records and ventilator data systems. This feature supports continuous monitoring with reduced manual abstraction burden, facilitating more timely feedback to clinical teams and quality departments. In settings where resources for manual chart review are constrained, electronic surveillance also promotes broader adoption and potentially more comprehensive case capture, strengthening internal performance monitoring.[3]

Beyond feasibility and standardization, the VAE surveillance parameters can function as a quality metric for care delivered to mechanically ventilated patients. When applied systematically, they enable organizations to quantify and track meaningful episodes of respiratory deterioration during ventilation, thereby offering a target for prevention-focused quality improvement. The framework's value as a performance indicator is reinforced by its association with mortality rates. Surveillance-defined VAEs have been shown to correlate closely with adverse outcomes, including increased risk of death, suggesting that the events captured by this model are clinically consequential rather than trivial fluctuations in ventilator management.[3] This association strengthens the case for using VAE surveillance to identify high-risk patterns, evaluate prevention strategies, and support institutional accountability. In addition, because the framework is not restricted to a single presumed etiology such as pneumonia, it can stimulate multidisciplinary collaboration by encouraging teams to address a broad range of modifiable contributors to deterioration, including fluid balance, sedation practices, ventilator settings, mobilization, aspiration risk, and infection prevention measures. The surveillance process therefore provides a common language that can align nurses, physicians, respiratory therapists, pharmacists, and infection prevention specialists around shared improvement priorities, enhancing coordination in efforts to mitigate VAE occurrence.[3] Nevertheless, despite these operational and quality-improvement advantages, the VAE framework has notable limitations that require careful interpretation when applied in practice. A foundational concern is that some VAEs may reflect the intrinsic trajectory of critical illness rather than complications that are preventable or directly induced by mechanical ventilation. In many critically ill patients, worsening oxygenation and escalating ventilator requirements may represent progression of underlying disease processes such as severe pneumonia, evolving acute lung injury, cardiogenic or noncardiogenic pulmonary edema, or systemic inflammatory states. In such cases, surveillance-defined deterioration may be an expected manifestation of the patient's condition rather than an avoidable lapse in care. This limitation underscores the risk of overattributing causality to the ventilator itself and highlights the importance of contextual clinical interpretation when using VAE data for quality assessment and feedback [3].

Another important constraint relates to the framework's imperfect alignment with ventilator-associated pneumonia detection. The surveillance

criteria for VAEs demonstrate a relatively low positive predictive value for VAP and may fail to identify some VAP cases.[3][4] This mismatch is significant because VAP has historically been a focal point of ventilator-related harm prevention efforts, and clinicians may assume that a surveillance system designed around ventilator complications should reliably track pneumonia events. However, VAEs are intentionally broader and structured to prioritize objective ventilator deterioration markers; as a result, the categories may capture many events driven by noninfectious causes, while missing clinically suspected pneumonia that does not produce the specific pattern or degree of oxygenation worsening required by the surveillance thresholds. This limitation can complicate efforts to use VAE rates as a surrogate for VAP performance and may contribute to misunderstanding if surveillance results are interpreted as direct indicators of pneumonia incidence. In addition, the historical VAP parameters themselves were frequently criticized for limited specificity in distinguishing VAP from other respiratory illnesses in critically ill patients, including other forms of potentially hospital-acquired infection or inflammation.[3][4] Radiographic abnormalities, fever, leukocytosis, purulent secretions, and deteriorating oxygenation may occur in a range of pulmonary conditions common in the ICU, such as atelectasis, pulmonary contusion, acute respiratory distress syndrome, aspiration pneumonitis, and fluid overload. The nonspecificity of these features contributed to the variability that the CDC's revised VAE model sought to address, yet it also means that the relationship between VAE surveillance categories and true infectious pneumonia is inherently complex. Consequently, while the VAE model may strengthen surveillance consistency, it cannot be assumed to provide a definitive representation of pneumonia epidemiology. Clinicians and quality leaders must therefore avoid conflating surveillance categories with diagnosis, and should interpret VAE trends alongside microbiologic data, clinical assessments, and local diagnostic practices [3][4].

Within the CDC's 2013 framework, ventilator-associated events are categorized into structured tiers that reflect increasing likelihood of infection-related pathology. The first tier, ventilator-associated conditions (VAC), captures sustained worsening in oxygenation after a period of stability or improvement, based on defined increases in ventilator support requirements. This category is intentionally broad and may encompass both infectious and noninfectious causes of deterioration. The second tier, infection-related ventilator-associated complications (IVAC), narrows the surveillance focus by incorporating indicators consistent with infection or inflammation—such as abnormalities in temperature or white blood cell count—and the initiation of new antimicrobial therapy, thereby suggesting an infectious contribution to the ventilator-associated decline. The third tier further refines surveillance toward pneumonia by identifying possible ventilator-associated pneumonia (PVAP) or probable ventilator-associated pneumonia (VAP) when additional evidence supports lower respiratory tract infection, often incorporating microbiologic criteria.[5] This tiered approach aims to preserve objectivity while acknowledging that not all respiratory deterioration during ventilation is infectious in origin, and that increasing diagnostic certainty requires additional, increasingly specific criteria. Overall, the CDC's 2013 VAE surveillance framework represents a deliberate shift toward standardized, measurable, and electronically tractable definitions intended to support population-level monitoring and quality improvement rather than individual clinical decision-making. Its advantages—objectivity, electronic feasibility, utility as a quality metric, association with mortality, and facilitation of multidisciplinary prevention efforts—are substantial and have encouraged wide implementation.[3] At the same time, its limitations—particularly the possibility of capturing the natural course of critical illness, the imperfect correspondence with VAP detection, and the enduring diagnostic ambiguity surrounding ICU respiratory syndromes—necessitate cautious interpretation.[3][4] When used appropriately, VAE surveillance can provide valuable insight into the burden of ventilator-associated deterioration and help direct systematic improvement. However, its findings should be integrated with clinical context and complementary data sources to ensure that performance evaluation and prevention strategies remain accurate, fair, and patient-centered [3][4].

VAC

Ventilator-associated conditions (VAC) constitute the initial tier within the CDC's ventilator-associated event (VAE) surveillance construct and are intended to capture clinically meaningful deterioration in oxygenation that occurs after a period of relative stability during mechanical ventilation. Within this framework, VAC is operationalized as a sustained escalation in oxygen requirements lasting for at least two consecutive days in a patient receiving invasive mechanical ventilation. In VAE surveillance terminology, "Day 1" corresponds to the calendar day on which endotracheal intubation occurs and mechanical ventilation is initiated. The defining feature of VAC is therefore not transient fluctuation, but rather a persistent change indicating worsening respiratory status. This sustained decline is identified through quantifiable ventilator parameters and is deemed present when there is either an increase in the daily minimum baseline positive end-expiratory pressure (PEEP) of at least 3 cm H2O or an increase in the daily minimum fraction of inspired oxygen (FiO2) of at least 20 percentage points, with either threshold maintained for a minimum of two days.[5] A critical safeguard embedded in the VAC definition is the requirement that deterioration must be preceded

by a demonstrable period of stability or improvement, ensuring that the surveillance signal reflects a new adverse event rather than initial instability associated with early critical illness or the immediate post-intubation phase. Accordingly, VAC may only be assigned to patients who have been mechanically ventilated for at least two days, and only when their oxygenation status has shown preexisting stability or improvement before the onset of the sustained increase in ventilatory support. In practical surveillance terms, this prerequisite is met when the patient demonstrates at least two days during which the daily minimum FiO2 or PEEP is stable or decreasing while on the ventilator. This interval functions as the "baseline" reference period against which subsequent worsening is judged, thereby enhancing consistency and reducing misclassification. During the period of stability or improvement, baseline FiO2 and baseline PEEP are defined using the minimum daily FiO2 and PEEP values recorded across that interval. The subsequent identification of VAC therefore depends upon comparing these baseline minima to the later, persistently increased daily minima, rather than relying on isolated peaks or clinician-selected reference points.[5]

The conceptual rationale for this approach is to privilege objective, reproducible measurements that can be applied uniformly across institutions and that lend themselves to electronic extraction. By anchoring VAC in daily minimum ventilator settings, the framework seeks to mitigate the influence of momentary adjustments, procedural interventions, or short-lived hypoxemic episodes that may not represent sustained physiologic decline. Nevertheless, while VAC surveillance captures episodes of durable respiratory worsening, the designation is etiologically nonspecific by design. A VAC episode can be driven by diverse processes, including infectious pneumonia, atelectasis, pulmonary edema, aspiration, evolving acute lung injury, or other complications of critical illness. Thus, VAC should be understood as a standardized surveillance marker of clinical deterioration in ventilated patients rather than as a diagnostic label indicating a particular pathology.[5] Infection-related ventilator-associated complications (IVAC) represent the subsequent tier of the CDC's VAE surveillance hierarchy and are intended to identify those VAC episodes that are plausibly attributable to infection or systemic inflammatory processes. IVAC is not defined independently of VAC; rather, it is predicated on the presence of VAC accompanied by clinical and therapeutic indicators that suggest an infectious contribution. The surveillance logic underlying IVAC is that when sustained ventilator deterioration occurs together with systemic signs consistent with infection and a clinician decision to commence antimicrobial treatment, the likelihood increases that an infectious process is implicated. Within this framework, the minimum duration of mechanical ventilation required before IVAC can be assessed is extended to three days, reflecting the expectation that infection-related ventilator complications typically emerge after a longer exposure window. Additionally, the required infection indicators must occur in a defined temporal relationship to the VAC episode, specifically within the two days preceding or the two days following the date of VAC assessment, thereby aligning physiologic worsening with contemporaneous evidence of infection.[5]

The infection indicators used for IVAC determination are explicitly defined to preserve surveillance objectivity. Temperature abnormalities constitute one required element and may be expressed either as low-grade fever, defined as a temperature greater than 100.4 °F (38 °C), or as hypothermia, defined as a temperature below 96.8 °F (36 °C). A second required element is an abnormal white blood cell count suggestive of systemic inflammatory activation or suppression, operationalized as leukocytosis exceeding 12,000 cells/mm3 or leukopenia at or below 4,000 cells/mm3. In addition to these physiologic markers, IVAC surveillance requires evidence of clinician response consistent with suspected infection: the initiation of an antimicrobial agent that is subsequently continued for at least four days. This treatment criterion is intended to distinguish brief empiric exposure or peri-procedural prophylaxis from sustained antimicrobial therapy reflecting ongoing clinical concern.[5] Collectively, these requirements position IVAC as a surveillance category that bridges purely physiologic deterioration (VAC) and more infection-specific classifications, without asserting diagnostic certainty. Within the CDC hierarchy, the identification of VAC and IVAC is intended to raise concern for ventilator-associated pneumonia (VAP) and related lower respiratory tract infections, although the surveillance system remains distinct from clinical diagnostic pathways. The subsequent categories—possible ventilator-associated pneumonia (PVAP) and probable VAP—seek to incorporate laboratory and microbiologic evidence to enhance specificity for pulmonary infection. PVAP and probable VAP are defined only when IVAC is present and when additional testing supports the presence of infection in the respiratory tract. PVAP criteria include findings consistent with purulent respiratory secretions on microscopy, specifically the presence of at least 25 neutrophils and no more than 10 squamous epithelial cells on sputum examination, which is used as a proxy for lower respiratory tract sampling quality and inflammatory burden. PVAP may also be satisfied by positive qualitative, semi-quantitative, or quantitative culture results obtained from specimens collected from the trachea, bronchi, or lung tissue, reflecting increasing microbiologic support for

infection.[5] Probable VAP is defined through more stringent culture-based thresholds, emphasizing quantitative microbial burden in samples obtained via established respiratory collection techniques. Under these criteria, probable VAP may be identified when endotracheal aspirate cultures yield at least 10^5 colony-forming units (CFUs) per milliliter, when bronchoalveolar lavage (BAL) cultures yield at least 10^4 CFU/mL, or when protected specimen brush sampling demonstrates at least 10^3 CFU/mL. These quantitative cutoffs aim to discriminate colonization from invasive infection by requiring higher organism density, thereby increasing the likelihood that detected pathogens are clinically relevant rather than contaminants or airway colonizers.[3][5] The framework also recognizes that certain microbiologic or pathologic findings may provide compelling evidence of infection even when routine respiratory cultures are equivocal. Consequently, PVAP or probable VAP determinations may be supported or superseded by a positive pleural fluid culture obtained via thoracocentesis, histopathologic confirmation of infection in lung tissue, or identification of specific respiratory pathogens such as Legionella or viruses including respiratory syncytial virus in respiratory secretions.[3][5] Taken together, VAC, IVAC, PVAP, and probable VAP comprise a tiered surveillance architecture that progresses from objective markers of ventilator-associated respiratory deterioration to increasingly infection-oriented criteria. This design reflects the CDC's intent to standardize event detection for surveillance and benchmarking while acknowledging the diagnostic complexity of respiratory decline in critically ill, mechanically ventilated patients. The system emphasizes reproducible ventilator metrics and defined clinical thresholds to enhance consistency across settings, yet it does not claim to substitute for individualized clinical assessment, imaging interpretation, or nuanced diagnostic reasoning at the bedside.[3][5]

Epidemiology

Epidemiologic descriptions of ventilator-associated events (VAEs) have expanded substantially since the introduction of the CDC's tiered surveillance definitions, enabling investigators to quantify not only ventilator-associated pneumonia (VAP) but also broader patterns of ventilator-related respiratory deterioration and infection-associated complications. In one large retrospective cohort study undertaken in 2013 at a tertiary academic center, the burden of VAE categories was evaluated across a sizeable population of mechanically ventilated patients. Among 20,356 individuals who required invasive ventilation, 5.6% (n=1141) met criteria for ventilator-associated conditions (VAC), 2.1% (n=431) satisfied infection-related ventilator-associated complication (IVAC) definitions, 0.7% (n=139) were classified as possible ventilator-associated pneumonia (PVAP), and 0.6% (n=127) met criteria for probable VAP.[6] These stratified proportions illustrate an important epidemiologic observation: as surveillance definitions become increasingly specific and require more stringent infection evidence, the number of qualifying cases predictably declines. This gradient is epidemiologically informative because it suggests that a substantial fraction of clinically significant respiratory deterioration during ventilation may not be attributable to pneumonia alone, but rather to a broader set of infectious and noninfectious processes captured at the VAC level. The same 2013 cohort study also demonstrated meaningful variation in VAE risk across hospital unit types, highlighting the influence of case mix, procedural exposure, and patient acuity on event distribution. The risk of VAC was reported to be highest among medical, surgical, and thoracic units, whereas cardiac and neuroscience units exhibited the lowest observed risk.[6] Such differences likely reflect heterogeneous patient populations, including the prevalence of complex surgeries, trauma, systemic sepsis, and preexisting pulmonary vulnerability in certain units, in contrast to differing ventilatory pathways and postoperative trajectories in others. Importantly, the study's unit-level distribution further emphasized the concentration of events in surgical and medical services. Forty-two percent (42%) of VAC and IVAC cases originated from surgical units, while 29% arose from medical units.[6] This pattern suggests that surgical environments, where patients often face increased exposure to operative stress, transfusion, fluid shifts, and perioperative aspiration risk, may represent a particularly important target for preventive strategies, while medical units continue to contribute a substantial share due to high burdens of respiratory failure, sepsis, and chronic comorbidity [6].

Microbiologic characterization within the same cohort provided additional insight into the infectious component of VAEs, particularly among those meeting IVAC and probable VAP criteria. Among cases of IVAC and probable VAP, Staphylococcus aureus was the most frequently implicated organism (29%), followed by Pseudomonas aeruginosa (14%) and Enterobacter species (7.9%).[6] The prominence of these pathogens is consistent with the established ecology of hospital-acquired lower respiratory infections in critically ill populations, including the frequent role of gram-positive cocci such as S. aureus and the clinically challenging burden of nonfermenting gram-negative organisms such as P. aeruginosa. These microbiologic patterns have epidemiologic importance because they shape empiric antimicrobial decision-making at a population level and underscore the role of local antibiograms, infection prevention practices, and device-care bundles in influencing pathogen distribution and resistance profiles. From a surveillance standpoint, the organism profile also

supports the conceptual validity of higher-tier VAE categories as markers of clinically significant infection rather than mere physiologic deterioration. Beyond incidence and microbiology, the 2013 study reinforced the adverse outcome profile associated with VAEs. Overall, VAE occurrence was linked to delays in extubation, longer hospitalization, and elevated mortality risk.[6] These associations are epidemiologically consequential because they indicate that VAEs function not only as surveillance markers but also as prognostic signals of complicated clinical courses. A greater number of days to extubation suggests impaired readiness for ventilator liberation and potentially greater exposure to sedation, immobility, and airway instrumentation, all of which can compound risk. Similarly, prolonged length of stay reflects downstream consequences such as additional diagnostic workup, escalation of respiratory support, treatment of infection or inflammation, and rehabilitation needs. The association with higher mortality emphasizes that VAE categories, even when defined for surveillance rather than diagnosis, capture episodes that correlate with severe physiologic decline and are therefore relevant to patient safety initiatives. Comparable epidemiologic and outcome signals were reported in a later single-center retrospective cohort study conducted in 2017 within the general intensive care unit of an academic hospital in Tokyo, Japan. In this study, 407 adult patients who were mechanically ventilated for at least four days were evaluated, thereby focusing on a subgroup with prolonged exposure to ventilatory risk.[7] Mortality was reported to be higher among patients meeting VAC and IVAC criteria (in the absence of VAP) when compared with patients who experienced neither VAE nor VAP.[7] This finding is important epidemiologically because it suggests that VAC and IVAC capture clinically meaningful deterioration even when pneumonia criteria are not met, reinforcing the conceptual shift from a pneumonia-centered model to a broader event-based surveillance approach. The report that VAC and IVAC were independently associated with higher mortality further strengthens the inference that these categories are not simply administrative artifacts, but rather markers of patient trajectories that are materially worse than those of mechanically ventilated patients without such events.[7] It also implies that prevention efforts aimed at reducing VAC and IVAC may have the potential to influence outcomes even beyond classical VAP prevention, by targeting noninfectious etiologies of deterioration such as fluid overload, atelectasis, ventilator-induced lung injury, or aspiration [6][7].

At the national population level, the burden of hospital-acquired pneumonia (HAP) and VAP has been highlighted as a major component of hospital-acquired infections (HAIs). A multistate survey conducted in the United States in 2014 reported that HAP and VAP together represent two of the most common categories of HAIs and account for 22% of all HAI cases.[8] This proportion conveys the substantial frequency of respiratory infections in healthcare settings and emphasizes the importance of infection prevention measures that target airway management, aspiration prevention, oral care, and ventilator circuit practices. From an epidemiologic perspective, the high share of HAIs attributable to pneumonia reflects not only the intrinsic vulnerability of hospitalized patients—particularly those requiring critical care—but also the significant exposure risk associated with invasive respiratory devices. Such national estimates underscore why surveillance systems and prevention bundles for ventilated patients remain central to patient safety agendas. Economic epidemiology has further clarified the substantial cost burden associated with VAP and other major HAIs. A meta-analysis published in 2013 focused exclusively on studies conducted in the United States between 1986 and 2013, synthesizing evidence on the financial impact of five major HAIs.[9] In this analysis, VAP was identified as the second largest contributor to total annual costs, accounting for 31.6% of the combined annual cost burden, which was estimated at $9.8 billion (95% CI, $8.3–$11.5 billion). Surgical-site infections ranked first, contributing 33.7% of the overall cost.[9] The positioning of VAP immediately behind surgical-site infections is epidemiologically meaningful because it reflects both the frequency of VAP and the resource intensity associated with its management, including prolonged ventilation, additional antimicrobial therapy, diagnostic imaging, microbiologic evaluation, and extended ICU care. These costs also have broader system-level implications, as they affect bed capacity, staffing requirements, and the allocation of high-acuity resources. While available studies provide valuable insight into the epidemiology and consequences of VAEs, important gaps remain, particularly regarding global patterns and the distribution of events across diverse economic contexts. The bulk of high-resolution surveillance and cost analyses has been concentrated in higher-income settings with robust electronic health record infrastructures and established infection prevention surveillance programs. As a result, the epidemiology of VAEs in low-to-middle-income countries, and the extent to which VAE incidence, pathogen distributions, antimicrobial practices, and outcomes differ compared with higher-income countries, remains insufficiently characterized. Variation in ICU capacity, nurse-to-patient ratios, diagnostic access, antimicrobial stewardship resources, and baseline disease burden may all influence both measured incidence and clinical outcomes. Consequently, further research is needed to clarify the global epidemiology of VAEs and to support context-

sensitive prevention and surveillance strategies that can be implemented effectively across health systems with different resource profiles.[6][7][8][9]

Issues of Concern

Intubation-related Complications

Critically ill patients who require invasive mechanical ventilation generally undergo endotracheal intubation via the oral or nasal route, a procedure that is fundamental to airway protection and ventilatory support yet intrinsically associated with procedural risk. Intubation is frequently performed under urgent or emergent conditions in physiologically unstable patients, and this context alone amplifies the likelihood of adverse events. Complications may arise from technical difficulty, time pressure, altered anatomy, or the patient's limited cardiopulmonary reserve. A particularly consequential procedural hazard is failure to secure the airway on the first attempt, necessitating repeated laryngoscopy or alternative approaches. Each additional attempt tends to increase the probability of adverse outcomes, both by prolonging apnea time and by compounding airway trauma, thereby establishing multiple-attempt intubation as a recognized risk amplifier within airway management.[10] The spectrum of intubation-related complications is broad and includes both immediate life-threatening events and delayed sequelae. Difficulty with intubation can manifest as poor visualization of the laryngeal inlet, inability to advance the tube, or inadequate ventilation between attempts. Reflex airway responses such as laryngospasm and bronchospasm may occur, contributing to airway obstruction and further impairing oxygenation. Mechanical obstruction of the tube itself, whether from kinking, secretions, blood, or manufacturing defects, can also compromise ventilation, as can occlusion by patient biting in inadequately sedated individuals. Incorrect tube placement represents another major category of harm, including inadvertent right mainstem bronchial intubation, which can result in unilateral ventilation and atelectasis of the contralateral lung, or esophageal intubation, which can rapidly precipitate severe hypoxemia and hemodynamic collapse if not promptly recognized. Even after successful placement, tube dislodgement may occur during patient movement, transfers, agitation, or suctioning, potentially leading to abrupt loss of airway control. Aspiration—either during the intubation process or due to impaired airway reflexes—can introduce contaminated material into the lower respiratory tract and initiate chemical pneumonitis, bacterial infection, or progression to ventilator-associated pneumonia (VAP).[10] Physiologic complications such as severe hypoxia and profound hypotension are particularly important in critically ill populations, in whom a brief period of inadequate ventilation or a surge in sympathetic stimulation can trigger rapid deterioration. Sedative and induction agents may contribute to hypotension through vasodilation and myocardial depression, while positive pressure ventilation can reduce venous return and exacerbate shock states. In parallel, mechanical trauma to the oropharynx, dentition, pharynx, larynx, and trachea may occur as a direct consequence of instrumentation, with potential for bleeding, edema, and subsequent airway compromise. Some injuries carry longer-term consequences, including hematoma formation, tracheal stenosis, or necrosis, particularly when cuff pressure is excessive or when prolonged intubation contributes to mucosal ischemia. Additional infectious complications can develop in the upper airway following intubation, including sinusitis—especially with nasotracheal tubes—upper respiratory tract infection, and tracheobronchitis. These conditions may serve as precursors to lower respiratory tract infection and VAP, reinforcing that intubation-related harm is not confined to the time of tube insertion but may evolve throughout the period of airway device dependence.[10]

Ventilator-induced Lung Injury (VILI)

Beyond intubation itself, invasive mechanical ventilation carries the risk of ventilator-induced lung injury (VILI), a phenomenon in which the mechanical forces applied to the respiratory system produce or amplify structural and inflammatory lung damage. Contemporary descriptions typically organize VILI into four primary mechanistic pathways: atelectrauma, barotrauma, volutrauma, and biotrauma.[1] Although these mechanisms are conceptually distinct, they frequently overlap in clinical practice, reflecting the complex interaction between ventilator settings, lung recruitability, regional compliance, and the underlying disease state. The unifying principle is that injured or heterogeneous lungs exposed to repetitive mechanical stress may sustain further damage even when ventilation is necessary for survival, making protective strategies central to modern critical care.

Atelectrauma

Atelectrauma refers to injury generated by repetitive opening and closing of unstable or recruitable lung units, producing high shear stress at the interfaces between aerated and collapsed regions.[1][11] When alveoli repeatedly collapse during expiration and are forcibly reopened during subsequent inspiration, the resulting shear forces can disrupt epithelial and endothelial integrity, promote capillary leak, and initiate microinjury that may propagate inflammation. The pathophysiology is often described in terms of "stress concentration," wherein mechanical energy is not evenly distributed across the lung but is focused at vulnerable junctions, particularly where air boluses meet collapsed or fluid-filled airways. In this setting, the mechanical trauma is not merely a byproduct of pressure delivery; it is fundamentally related to cyclic recruitment dynamics that subject delicate alveolar

structures to recurrent deformation.[1][11] The propensity for atelectrauma is exacerbated by lung inhomogeneity, a defining characteristic of many critical respiratory syndromes. Alveoli do not function as isolated units; rather, they are mechanically interdependent through shared interalveolar septae. When one alveolus becomes atelectatic or fluid-filled, the septum between it and an adjacent aerated alveolus tends to deviate toward the collapsed or nonaerated space. This deviation distorts neighboring alveoli and produces nonuniform inflation patterns during mechanical ventilation, generating abnormal shear forces and uneven regional strain.[1][11] The consequences of such inhomogeneity include marked variability in regional lung mechanics and a reduction in the effective lung volume available for safe ventilation. Clinically and radiographically, this heterogeneity may be appreciated on computed tomography (CT) as juxtaposed areas of well-aerated parenchyma adjacent to atelectasis or opacification, reflecting a patchwork distribution of compliance. Histologic correlates may include hyaline membrane formation, interstitial and alveolar edema, and sloughing of respiratory epithelium, findings that signify disruption of the alveolar-capillary barrier. Conditions commonly associated with pronounced inhomogeneity include atelectasis, acute respiratory distress syndrome (ARDS), surfactant deficiency states, and pulmonary edema, all of which can heighten susceptibility to cyclic recruitment injury when ventilatory support is delivered without adequate attention to stabilizing end-expiratory lung volume.[1][11]

Barotrauma

Barotrauma classically describes injury that results from excessive pressure-related lung distension, culminating in air leak syndromes such as pneumothorax, pneumomediastinum, and subcutaneous emphysema.[1] To understand this mechanism, it is necessary to recognize the pressures required during inspiration. Each inspiratory cycle demands pressure to overcome airway resistance, accelerate airflow into the lungs, and counteract the elastic recoil of the respiratory system.[1] At the end of inspiration, a brief phase of no airflow occurs before expiration begins. During this pause, the distending force acting on the lung is best represented by transpulmonary pressure, generally conceptualized as the difference between alveolar airway pressure (often approximated by plateau pressure) and pleural pressure.[1] This distending pressure is central because it is the pressure actually applied across the lung tissue, and it is closely linked to lung volume changes and the risk of overdistension. In clinical practice, alveolar pressure at end inspiration can be approximated by the airway pressure measured during a period of zero flow, and plateau pressure reflects the airway pressure required to distend both the lung and chest wall when the patient is passive and not generating spontaneous breathing effort.[1] Pleural pressure, however, is difficult to measure directly and is often estimated via esophageal pressure monitoring, a method that may be technically cumbersome and may yield imprecise approximations. Consequently, plateau pressure is commonly used as a pragmatic surrogate to evaluate risk of overdistension, although it is an imperfect stand-in for true transpulmonary pressure.[1] This limitation becomes particularly important in patients with altered chest wall mechanics. When the chest wall is pathologically stiff, a substantial fraction of airway pressure may be expended in expanding the chest wall rather than distending the lung parenchyma. Under such circumstances, an elevated plateau pressure does not necessarily imply a proportionately elevated transpulmonary pressure, and therefore does not automatically indicate harmful lung overdistension. Interpretation of plateau pressure must thus be contextualized within the patient's underlying pathology, including obesity, abdominal hypertension, thoracic restriction, or other factors that modify chest wall compliance.[1] Barotrauma occurs when excessive lung inflation pressure generates high transpulmonary pressures that produce regional overdistension and subsequent air leakage.[1] The injury is often focal, reflecting heterogeneity in lung compliance, where relatively normal lung units may become disproportionately distended when adjacent regions are collapsed or consolidated. This phenomenon can culminate in alveolar rupture, allowing air to track into the pleural space, mediastinum, or subcutaneous tissues. Preventive strategies therefore emphasize meticulous control of inspiratory pressures, aiming to limit excessive distending forces while maintaining adequate gas exchange. Notably, the relationship between airway pressure and injury is not absolute; extremely low or negative pleural pressures—such as those generated by vigorous spontaneous inspiratory effort—may contribute to high transpulmonary pressures even when airway pressures appear modest, thereby enabling barotrauma at comparatively low measured airway pressures.[1] This nuance reinforces that barotrauma risk is determined by the interaction between ventilator-delivered pressures and patient-generated forces, as well as by the distribution of stress within a heterogeneously injured lung.

Volutrauma

Volutrauma describes lung injury that arises primarily from excessive alveolar distension during mechanical ventilation, emphasizing that the magnitude and distribution of delivered volume can be as injurious as elevated pressures. When alveolar units are exposed to mechanical hyperinflation, the epithelial lining experiences substantial strain. At a cellular level, this strain initiates adaptive repair responses intended to preserve membrane integrity.

One described mechanism involves mobilization of lipid components toward the alveolar plasma membrane, facilitating structural reinforcement and repair in the face of stretching forces. In effect, the cell increases its functional surface area to accommodate deformation, thereby reducing the likelihood of immediate membrane rupture. These protective responses, however, are finite and may become progressively overwhelmed when strain is sustained or intensified. Under conditions of escalating cellular stress, the integrity of membrane–cytoskeletal attachments may fail, and cells may detach from their anchoring structures. The physiologic consequences extend beyond epithelial compromise, because the alveolar-capillary barrier depends on intact junctions between alveolar epithelium and vascular endothelium. Once these junctional complexes break down, permeability increases, allowing fluid movement into the interstitium and alveolar spaces, thereby promoting interstitial and alveolar edema and further impairing gas exchange.[1][11] In this manner, volutrauma becomes both a structural injury process and a driver of worsening respiratory failure, particularly when overdistension is concentrated in relatively compliant, recruitable regions adjacent to collapsed or consolidated units.

Biotrauma

Mechanical injury to the lungs does not remain a localized mechanical phenomenon; it can also precipitate an exaggerated inflammatory cascade known as biotrauma. In this context, the physical forces associated with ventilation—especially when they produce overdistension or cyclic opening and closing—activate inflammatory signaling pathways and stimulate the release of injurious cytokines and related mediators. These inflammatory responses may develop within both diseased and comparatively normal regions of the lung, highlighting that injury is not confined exclusively to the most visibly affected parenchyma. The downstream effects can be systemic. Because the lungs possess an exceptionally large epithelial surface area and receive the entire cardiac output, even a modest localized inflammatory response has the potential to generate a substantial mediator burden capable of entering the bloodstream. Once disseminated hematogenously, these mediators may contribute to inflammatory injury in distant organs, thereby promoting multi-organ dysfunction and increasing mortality risk.[1][11] This systemic reach is central to the concept of biotrauma: ventilation-associated lung injury can act as a catalyst for whole-body inflammation, amplifying the severity of critical illness. Vulnerability to biotrauma is not uniform across patients. Individuals with concomitant physiologic stress—such as sepsis, trauma, postoperative inflammation, or chronic comorbidity—may already exist in a pro-inflammatory or immune-dysregulated state. In such settings, mechanical injury can serve as a trigger that escalates an already unstable immune response, producing a cascading inflammatory pattern that magnifies tissue damage. Thus, biotrauma is best understood as an interaction between mechanical stressors and host susceptibility, where ventilation-related strain provides the initiating stimulus and the patient's baseline inflammatory milieu influences the magnitude and consequences of the response.[1][11]

"Baby lung" of Acute Respiratory Distress Syndrome (ARDS)

A central concept in the modern understanding of ARDS is the "baby lung," which refers to the reduced fraction of lung that remains effectively aerated and available for ventilation and gas exchange. In ARDS, surfactant dysfunction and pulmonary edema are common and contribute to collapse of dependent lung regions. As dependent areas become atelectatic and fluid-filled, the overall functional lung volume diminishes, meaning that the ventilator-delivered tidal volume is distributed over a smaller aerated lung mass than would be present in a healthy individual. This reduction in ventilatable lung volume is what the "baby lung" metaphor captures: the lungs behave as though they are physically smaller with respect to functional ventilation capacity. Dependent atelectasis is not necessarily fixed; rather, it may be partially redistributable with changes in body position. For example, when patients are placed in the prone position, anterior regions can become more affected, reflecting the shifting gravitational and mechanical forces that influence regional aeration.[11] The "baby lung" framework has important implications for ventilator settings. Because the functional lung volume is reduced, even conventional tidal volumes can produce disproportionately high regional strain and contribute to volutrauma in the remaining aerated units. Consequently, lower tidal volumes are frequently required in ARDS, not only to accommodate impaired compliance but also to reduce the risk of overdistension in the limited recruitable lung regions. It is also important to emphasize that recruitable regions in ARDS are not synonymous with normal lung. Even the aerated portions may exhibit structural and functional abnormalities, including inflammation, altered perfusion, and heterogeneity in compliance. As a result, protective ventilation in ARDS is not simply a matter of ventilating "healthy" residual lung gently; rather, it involves navigating a complex landscape of partially injured, variably recruitable tissue with the aim of preventing further iatrogenic harm.[11]

Therapeutic and Preventative Strategies for VILI

The objectives of mechanical ventilation have evolved beyond the historic priority of maintaining adequate oxygenation and carbon dioxide clearance with minimal work of breathing. Contemporary critical care recognizes that ventilation itself can contribute to lung injury and that preventing VILI is an essential therapeutic goal

alongside sustaining life. This shift requires ventilator settings to be selected not only for physiologic effectiveness but also for their potential to impose harmful mechanical forces. Accordingly, clinicians must continually balance anticipated benefits—such as improved gas exchange and reduced respiratory muscle workload—against the risk of inducing or exacerbating lung injury through overdistension, cyclic recruitment, and inflammation.[1] Several preventative strategies have been emphasized within this protective paradigm. Delivering lower tidal volumes is intended to limit regional overdistension, especially in heterogeneously injured lungs where compliant areas are at risk of receiving a disproportionate share of delivered volume. Increasing PEEP is often used to maintain end-expiratory lung volume and reduce cyclic alveolar collapse, thereby mitigating atelectrauma. Recruitment maneuvers, described as the delivery of sustained airway pressures exceeding 35 cm H2O, may be employed to reopen atelectatic lung units and improve aeration.[1] These approaches reflect a coherent physiologic logic: stabilizing alveoli and minimizing excessive strain should reduce structural injury and inflammatory activation. Yet, their effectiveness and safety depend heavily on patient-specific factors, including lung recruitability, hemodynamic reserve, and the presence of coexisting pathology. Notably, no universally ideal ventilation strategy has been established, and each intervention carries potential harms alongside benefits. For instance, lowering tidal volume may be necessary to reduce overdistension and mitigate auto-PEEP in certain patients, but this adjustment can also lead to impaired carbon dioxide clearance. The resulting rise in arterial partial pressure of CO2 may contribute to respiratory acidosis and, in susceptible patients, may increase intracranial pressure, thereby creating competing clinical priorities.[1] Similarly, while higher PEEP can prevent alveolar collapse and reduce atelectrauma, excessive PEEP may compromise venous return, reduce cardiac output, and produce hemodynamic instability. Moreover, overly high PEEP can itself contribute to regional overdistension and barotrauma if applied to lungs with limited recruitability.[1] Therefore, prevention of VILI is not achieved through rigid adherence to a single setting target but through individualized titration that accounts for physiology, comorbidities, and evolving risk profiles.

The rationale for low tidal volume ventilation is grounded in the observation that critically ill patients often exhibit dependent regions of reduced aeration, leaving a smaller proportion of normally aerated nondependent lung to receive the delivered tidal volume. In such circumstances, delivering a smaller tidal volume to the relatively aerated regions helps reduce the likelihood of excessive strain, thereby lowering the risk of volutrauma and pressure-related air leak syndromes.[1] This principle emphasizes that "normal" tidal volumes may become injurious when the functional lung is effectively reduced, as in the "baby lung" model. The titration of PEEP represents a similarly nuanced protective strategy. While low PEEP may fail to recruit collapsed alveoli and may permit ongoing cyclic collapse, thereby promoting atelectrauma, excessively high PEEP can impose hemodynamic burden and contribute to overdistension.[1] The clinical challenge is therefore to identify a PEEP level that optimizes recruitment and oxygenation while minimizing both mechanical injury and cardiovascular compromise. Measurement of transpulmonary pressure has been explored as a method to individualize PEEP by estimating the pressure actually distending the lungs; this approach has demonstrated benefits such as improved oxygenation and reduced mortality, but it has not become routine in standard practice, likely due to technical complexity and variability in measurement precision. Consequently, recruitment maneuvers and PEEP optimization remain largely guided by clinical judgment, integrating bedside assessments and an evolving evidence base, while awaiting more standardized approaches that reliably balance benefit and risk.[1] High-frequency oscillatory ventilation (HFOV) has also been proposed as a strategy to reduce VILI by delivering extremely small tidal volumes at very high frequencies, theoretically limiting alveolar stretch while maintaining ventilation. However, uncertainty regarding whether HFOV confers meaningful improvements in clinical outcomes has prevented its incorporation into routine standard practice.[1] This uncertainty underscores the broader principle that physiologic plausibility alone is insufficient; ventilation strategies must demonstrate consistent outcome benefits without unacceptable harm. Overall, protective ventilation is best conceptualized as a dynamic, patient-centered process that integrates low-strain principles, stabilization of recruitable lung units, and vigilant assessment of systemic consequences, rather than as a fixed protocol applied uniformly to all ventilated patients.[1]

Adjunctive Strategies to Prevent VILI

Adjunctive strategies to reduce ventilator-induced lung injury (VILI) are often deployed when conventional lung-protective ventilation alone is insufficient to achieve adequate gas exchange without imposing injurious mechanical stress. These approaches are best understood as supportive measures that modify the physiologic context in which mechanical ventilation is delivered. Rather than replacing lung-protective settings, they aim to decrease the intensity of mechanical forces required for ventilation, improve the homogeneity of regional ventilation, or mitigate downstream inflammatory and systemic consequences. In contemporary

practice, the decision to employ such interventions typically reflects a careful appraisal of competing risks: the hazards of ongoing hypoxemia or hypercapnia, the mechanical burden of ventilation on vulnerable lung tissue, and the possibility that adjunctive measures may introduce new complications. Consequently, these strategies demand individualized integration into an overarching plan that balances oxygenation, ventilation, hemodynamics, and safety.[1] One proposed adjunct involves reducing metabolic demand with the intention of lowering the patient's physiologic requirement for oxygen uptake and carbon dioxide clearance. The conceptual rationale is straightforward: oxygen consumption and carbon dioxide production are tightly linked to cellular metabolic activity, and if systemic demand can be safely reduced, the required intensity of ventilatory support may decrease. In principle, this could allow clinicians to maintain lower tidal volumes, limit airway pressures, and reduce overall ventilatory work while still meeting metabolic needs. However, although the concept has been described as a therapeutic approach to preventing VILI, it remains insufficiently characterized within standard practice frameworks.[1] The practical challenges are substantial because metabolic demand is influenced by diverse factors such as fever, agitation, shivering, pain, and systemic inflammation. Interventions that suppress metabolism may involve deeper sedation, temperature modulation, or other measures that carry their own risks, including delirium, prolonged ventilation, immune suppression, or hemodynamic instability. Thus, while reduction of metabolic demand aligns with lung-protective goals, it has not been consistently operationalized as a standardized strategy in routine ICU care.[1]

Prone positioning represents one of the most clinically influential adjunctive interventions in severe hypoxemic respiratory failure and is widely discussed in the context of VILI prevention because of its capacity to improve oxygenation and potentially reduce mortality among mechanically ventilated patients.[1] The physiologic benefits of proning arise from a constellation of mechanisms that collectively enhance the efficiency and distribution of ventilation. When a patient is placed prone, end-expiratory lung volume may increase, contributing to better alveolar stability at end expiration. Ventilation of dependent lung regions can improve, in part because the prone position relieves compressive effects of the cardiac mass on the lower lobes, thereby expanding dorsal lung units that are often preferentially atelectatic in the supine position. Improvements in ventilation–perfusion matching may also occur, allowing oxygenation to rise without requiring escalation of FiO2 or injuriously high ventilator pressures. Additionally, prone positioning may decrease lung inhomogeneity by redistributing stress and strain more evenly across lung regions, potentially reducing localized overdistension and cyclic collapse that contribute to VILI.[1] Yet proning is not a benign maneuver and requires meticulous prevention of procedure-related complications. Airway dislodgement and obstruction represent critical risks because endotracheal tube integrity is essential in ventilated patients; similarly, sustained pressure on dependent tissues increases the risk of decubitus ulcers. Effective proning therefore depends on disciplined team coordination, secure airway management, protective padding, scheduled repositioning, and vigilant monitoring for device-related and skin complications.[1] Extracorporeal membrane oxygenation (ECMO) is another adjunctive modality that may be considered when conventional ventilation cannot maintain acceptable gas exchange without excessive mechanical stress. ECMO can be instituted partially or totally, and when used partially, it may reduce the complication burden associated with mechanical ventilation by enabling reductions in tidal volume requirements and other ventilator settings that contribute to lung strain.[1] By offloading a portion of oxygenation and/or carbon dioxide elimination to an extracorporeal circuit, clinicians may be able to implement more "ultra-protective" ventilation, thereby limiting volutrauma and barotrauma in severely injured lungs. However, the overall benefit and indications for ECMO in this context remain uncertain.[1] This uncertainty reflects not only questions about patient selection and timing but also the reality that ECMO itself carries significant risks, including bleeding, thrombosis, infection, vascular injury, and complications related to anticoagulation. Consequently, ECMO is typically reserved for carefully selected patients in centers with appropriate expertise and resources, and its use should be framed as a strategy to facilitate lung protection rather than as a universal escalation pathway.

Pharmacologic interventions have also been discussed as adjuncts to reduce VILI risk, primarily through optimizing patient–ventilator synchrony and moderating the inflammatory cascade associated with mechanical injury. Neuromuscular blockade is particularly relevant in patients with acute respiratory distress syndrome (ARDS), who may exhibit strong respiratory drive, dyssynchronous breathing patterns, or active resistance to ventilator-delivered breaths. By eliminating spontaneous respiratory effort, neuromuscular blocking agents can improve synchrony, stabilize ventilatory mechanics, and potentially reduce injurious swings in transpulmonary pressure associated with vigorous inspiratory efforts. This improved synchrony may decrease the risk of biotrauma and its systemic consequences, including multiorgan dysfunction and increased mortality.[1] Nevertheless, neuromuscular blockade must be approached cautiously, as prolonged paralysis can contribute to ICU-acquired weakness and complicate rehabilitation. Its role as a protective adjunct

therefore hinges on appropriate patient selection, time-limited use, and comprehensive supportive care, including sedation management and early mobilization strategies when feasible. Other pharmacologic approaches, including prophylactic anti-inflammatory agents and stem cell therapies, have been proposed as potentially beneficial in reducing the incidence or magnitude of biotrauma by dampening inflammatory mediator release or promoting tissue repair. However, these interventions are not well characterized and are not routinely implemented in standard practice.[1] The concept is mechanistically appealing given the centrality of inflammation to VILI progression, but limited clinical standardization reflects uncertainties regarding efficacy, safety, dosing, and the risk of immunomodulation in critically ill populations who are often already vulnerable to infection and immune dysregulation. Accordingly, these therapies remain largely investigational and should be viewed as emerging rather than established tools for VILI prevention.[1]

Oxygen toxicity represents an additional concern in ventilated patients, particularly when high fractions of inspired oxygen (FiO2) are required for sustained periods. Oxygen delivery is determined by FiO2 and duration of exposure, and toxicity arises through the generation of reactive oxygen species, notably superoxide, hydrogen peroxide, and hydroxyl radicals. These molecules can induce cellular injury, propagate inflammation, and contribute to adverse genetic alterations.[12] Despite extensive recognition of oxygen toxicity mechanisms, a clear consensus has not been established regarding a definitive safe threshold for inspired oxygen levels. As a result, the prevailing clinical recommendation is pragmatic: clinicians should use the lowest FiO2 that achieves adequate oxygenation.[12] In practice, this principle aligns with lung-protective goals because sustained hyperoxia may aggravate alveolar injury and inflammatory signaling, potentially worsening pulmonary dysfunction and increasing dependence on mechanical ventilation. Thus, FiO2 titration should be approached not only as a means of meeting oxygenation targets but also as a long-term safety strategy that limits oxidative stress. Auto-positive end-expiratory pressure (auto-PEEP), also described as intrinsic PEEP or air-stacking, is a mechanically mediated phenomenon that can meaningfully influence both VILI risk and hemodynamic stability. Under resting conditions in healthy individuals, the elastic recoil forces of the lung and chest wall reach equilibrium at end expiration, and end-expiratory lung volume (EELV) approximates the relaxation volume (V), resulting in an absence of end-expiratory airflow. In some mechanically ventilated patients, however, end-expiratory airflow remains above zero even without sustained active expiration.[13] This persistent airflow indicates incomplete emptying of the lungs before the next inspiratory cycle begins, meaning that EELV exceeds the relaxation volume. When EELV increases above V, pulmonary hyperinflation is present, and each subsequent delivered tidal volume can further elevate EELV and end-inspiratory lung volume (EILV), producing progressive air-stacking.[13] As lung volume rises, airway diameter distends, and elastic recoil forces increase reciprocally, creating higher positive alveolar pressure at end expiration—the pressure-based counterpart of the volume-based hyperinflation. This combined process constitutes auto-PEEP and is associated with elevated expiratory flow as the respiratory system attempts to dissipate the stored elastic energy.[13]

Auto-PEEP is particularly prevalent in mechanically ventilated patients with obstructive or heterogeneous lung disease, including asthma and chronic obstructive pulmonary disease (COPD), but it may also occur in ARDS, acute respiratory failure, sepsis, and respiratory muscle weakness.[13] Multiple ventilator-mediated mechanisms can contribute, including reduced expiratory time, increased expiratory time constant, excessive minute ventilation, increased external airflow resistance, large tidal volume delivery, persistent inspiratory muscle activity during expiration, and increased lung compliance.[13] These mechanisms often converge in critically ill patients, where airway narrowing, secretions, ventilator settings, and patient–ventilator dyssynchrony interact to prevent complete exhalation. The respiratory consequences of auto-PEEP are clinically significant. Elevated EILV can cause alveolar overdistension and reduce lung compliance, thereby increasing the risk of barotrauma. Because higher elastic recoil must be overcome, the elastic work of breathing rises. In addition, patients may need to generate a more negative intrathoracic pressure—equal to the positive intra-alveolar pressure at end expiration—just to initiate inspiratory flow, which increases threshold work of breathing. Auto-PEEP can also impair respiratory muscle function, worsen ventilation distribution, and contribute to hypoxia through inhomogeneous delivery of inspired air across alveolar units, thereby undermining effective patient–ventilator interaction.[13] These effects can produce a cycle in which dyssynchrony and increased respiratory effort further worsen hyperinflation and mechanical stress.

Cardiovascular compromise is another major consequence of auto-PEEP because elevated intrathoracic pressure reduces venous return and preload, limiting cardiac filling. Auto-PEEP can increase pulmonary vascular resistance, thereby raising right ventricular afterload and impeding right ventricular outflow. The requirement for more negative intrapleural pressure to initiate inspiration may also increase left ventricular afterload, and the

cumulative impact can be a reduction in cardiac output.[13] In some circumstances, high positive pressure ventilation can elevate intrathoracic pressure sufficiently to reduce venous drainage from the head, increasing intracranial pressure and potentially contributing to delirium or agitation.[13] These systemic effects emphasize that auto-PEEP is not merely a ventilator waveform abnormality; it is a physiologically consequential state that can destabilize multiple organ systems. Recognition and monitoring of auto-PEEP rely on both ventilator-derived and clinical indicators. Persistent end-expiratory airflow on the ventilator monitor is a key sign when hyperinflation is present, and a wheeze persisting to end expiration may be auscultated clinically. Additional cues include poor patient–ventilator synchrony, pulsus paradoxus, variability in pulse oximetry readings, elevated plateau pressures, and the development of hypotension, all of which may prompt suspicion of significant intrinsic PEEP.[13] Management strategies must be tailored to the underlying mechanism and are influenced by whether ventilation is delivered in volume-controlled or pressure-controlled modes. Adjustments may include modifications to respiratory rate, tidal volume, minute ventilation, inspiratory time, and heat moisture exchange filtration to improve expiratory time and reduce airflow resistance. Supportive measures such as ensuring adequate analgesia and temperature control may reduce excessive respiratory drive, and bronchodilator therapy may be applied when clinically indicated. In some cases, careful application of low-level external PEEP may help mitigate triggering work and improve synchrony, while intravascular fluid expansion may be needed to preserve hemodynamic stability. Severe hypotension attributable to auto-PEEP may require prompt ventilator disconnection to allow lung deflation, followed by reconnection once the patient stabilizes; if hypotension does not respond to disconnection, tension pneumothorax should be suspected.[13] Ultimately, there is no single standardized intervention for auto-PEEP, and treatment must be individualized based on patient physiology, comorbidities, and the evolving risk profile, consistent with a holistic approach to preventing VILI and its systemic complications.[13]

Ventilator-associated Pneumonia (VAP)

Ventilator-associated pneumonia (VAP) remains one of the most clinically consequential infectious complications encountered in the intensive care setting, and its prevention, recognition, and management continue to occupy a prominent position in critical care practice and policy. Guidance from professional societies has sought to standardize how clinicians conceptualize and approach VAP, while also acknowledging persistent diagnostic uncertainty and the growing challenges posed by antimicrobial resistance. In 2005, the American Thoracic Society (ATS) and the Infectious Diseases Society of America (IDSA) jointly issued comprehensive guidance addressing the management of hospital-acquired pneumonia (HAP) and VAP.[14] Although these recommendations were updated in 2016, the ATS and IDSA explicitly maintained that the definitional constructs for HAP and VAP presented in the 2005 document retained clinical relevance and practical applicability; consequently, the core definitions were not revised in the later update.[15] This continuity underscores a broader reality in critical care infectious diseases: while evidence and therapeutic options evolve, certain definitional anchors remain stable because they reflect durable clinical patterns and operational needs. Within the ATS/IDSA framework, VAP is defined as pneumonia that develops more than 48 hours after the initiation of mechanical ventilation.[14] This temporal threshold is intended to differentiate infections arising in association with ventilatory support from community-acquired or preexisting pulmonary infections that were present before intubation. Accordingly, a defining premise of VAP diagnosis is that clinical features compatible with pneumonia should not have been evident prior to, or at the time of, endotracheal intubation. Pneumonia itself is conceptualized through a combination of radiographic and clinical evidence. Radiographically, the presence of a new lung infiltrate is required, while clinical indicators suggestive of an infectious etiology include new-onset fever, purulent sputum, leukocytosis or leukopenia, and deterioration in oxygenation.[14] These criteria reflect the multifactorial nature of pneumonia assessment in the ICU, where imaging and physiologic data must be interpreted against a background of competing diagnoses such as atelectasis, pulmonary edema, acute respiratory distress syndrome (ARDS), pulmonary hemorrhage, and aspiration pneumonitis.

The temporal dimension of VAP has further been refined into early-onset and late-onset categories to support prognostication and therapeutic decision-making. Early-onset VAP is generally considered to occur within the first 96 hours of mechanical ventilation and has been associated with a more favorable prognosis.[14] Late-onset VAP, arising after the first 96 hours, is associated with higher mortality risk and an increased probability of infection due to multidrug-resistant (MDR) organisms.[14] These distinctions reflect epidemiologic observations that prolonged ICU exposure increases colonization pressure, antibiotic exposure, and the opportunity for cross-transmission, all of which shift the microbial ecology toward more resistant phenotypes. Notwithstanding the early/late categorization, VAP overall is consistently associated with substantial morbidity and mortality, mediated through prolonged ventilation, systemic inflammation, sepsis, and the downstream consequences of critical illness deconditioning.[14] It is essential to differentiate VAP from hospital-acquired pneumonia (HAP), which

represents a distinct nosologic entity. HAP is defined as pneumonia that is not present at the time of hospital admission but develops two or more days after admission.[14] Unlike VAP, HAP does not require the presence of mechanical ventilation and may occur in non-ventilated patients, including those on general wards or in step-down settings. This distinction is clinically relevant because the exposure profiles, diagnostic constraints, microbial risks, and prevention strategies may differ between ventilated and non-ventilated populations, even though overlap exists in pathogen spectra and in the influence of institutional ecology.

Despite the importance of accurate identification, the diagnosis of VAP remains challenging because there is no universally accepted gold standard.[15] The ATS/IDSA 2016 guideline, while acknowledging diagnostic complexity, recommends a practical diagnostic approach based on clinical criteria alongside non-invasive respiratory sampling with semiquantitative cultures.[15] In this context, non-invasive sampling refers primarily to endotracheal aspiration of respiratory secretions. Under the recommended approach, a positive culture result is defined broadly as any amount of pathogenic microbial growth, a position that reflects the realities of ICU diagnostics where airway colonization and infection can be difficult to separate with certainty, and where the urgency of clinical decision-making often necessitates acting on imperfect information.[15] In contrast, invasive sampling involves techniques such as blind bronchial sampling or bronchoscopy-directed procedures including bronchoalveolar lavage (BAL) or protected specimen brush (PSB) sampling. These methods are frequently paired with quantitative culture interpretation, using colony-forming unit (CFU/mL) thresholds, and the laboratory diagnostic cutoffs correspond to those previously outlined in surveillance definitions.[15] The distinction between non-invasive and invasive strategies is not merely technical; it reflects trade-offs between feasibility, risk, timeliness, and diagnostic specificity, especially in physiologically unstable patients. The guideline further emphasizes that diagnostic reasoning for VAP should not rely solely on cultures or imaging but should incorporate broader clinical context. Considerations include the possibility that infection originates from an alternative source, the overall degree of clinical suspicion, the presence of sepsis, prior exposure to antimicrobial therapy at the time the culture specimen is obtained, and evidence of clinical response to antimicrobial treatment.[15] These factors matter because prior antibiotics can suppress culture yield, sepsis can have multiple potential foci, and radiographic changes may lag behind clinical course. Likewise, improvement after antimicrobial therapy may support an infectious diagnosis, though it does not prove it, because supportive ICU interventions and the natural trajectory of noninfectious inflammation may also produce apparent clinical gains.

Among tools intended to structure clinical assessment, the Clinical Pulmonary Infection Score (CPIS) has been proposed as a means to aggregate multiple indicators into a composite estimate of VAP likelihood. CPIS incorporates elements such as body temperature, leukocyte count and morphology, microbiologic findings from respiratory culture, oxygenation status as inferred from the arterial partial pressure of oxygen to inspired oxygen fraction ratio, and chest radiography findings.[16] A CPIS of six or greater out of a maximum of twelve has been interpreted as indicating a high probability of VAP.[16] The score's appeal lies in its ability to standardize assessment and potentially facilitate earlier identification in ambiguous cases. However, its limitations are also well recognized: CPIS demonstrates restricted sensitivity and specificity and is subject to interobserver variability, particularly because radiographic interpretation and secretion assessment are inherently subjective. Consequently, CPIS may be useful as a screening adjunct, but it cannot substitute for clinical judgment and comprehensive evaluation.[16] From an etiologic standpoint, contemporary concerns increasingly focus on the rising prevalence of VAP due to MDR or extremely drug-resistant (XDR) pathogens. Organisms of particular concern include Pseudomonas aeruginosa, Acinetobacter species, Enterobacter species, Staphylococcus aureus, and Klebsiella pneumoniae.[17] These pathogens are typically hospital-acquired and collectively account for an estimated 80% of VAP cases.[17] This epidemiology has substantial implications for empiric therapy selection and for infection prevention priorities because resistant gram-negative bacilli and MRSA can substantially narrow effective therapeutic options, delay appropriate therapy when initial regimens are inadequate, and increase the risk of toxicity from salvage agents. Risk factors for VAP reflect both patient vulnerability and exposure intensity. Advancing age, the presence of comorbid conditions, prolonged ICU or hospital length of stay, extended duration of mechanical ventilation, and cumulative exposure to invasive procedures have all been identified as factors that increase VAP risk.[15][18] The relationship between VAP and airway instrumentation is particularly salient: intubation and prolonged presence of an endotracheal tube compromise normal airway defenses, impair mucociliary clearance, facilitate microaspiration around the cuff, and provide a surface for biofilm formation, all of which create an environment conducive to bacterial proliferation and infection.[15][18] These mechanisms help explain why reducing ventilator days and optimizing airway care are central to prevention strategies.

The ATS/IDSA 2016 guideline highlights specific risk factors associated with MDR VAP, recognizing that the likelihood of resistant pathogens should drive empiric coverage decisions.[15] Identified risk factors include prior intravenous antibiotic use within 90 days, septic shock at the time of VAP diagnosis, ARDS preceding VAP onset, hospitalization for five or more days prior to VAP development, and receipt of acute renal replacement therapy before VAP onset.[15] Additionally, prior antibiotic therapy and late onset of symptoms are described as prominent risk indicators for VAP due to methicillin-resistant Staphylococcus aureus (MRSA).[15] These risk factors are clinically important because they provide a structured basis for stratifying patients and tailoring initial antimicrobial regimens to balance timely effective therapy against the harms of unnecessary broad-spectrum exposure. Therapeutic management of VAP is complicated by the intersecting pressures of antimicrobial resistance, the potential harms of overtreatment, and the necessity of directing therapy toward the causative organisms.[15] The ATS/IDSA 2016 recommendations are evidence-based but explicitly framed as voluntary guidance to be applied at the discretion of attending physicians, and they do not supersede individualized clinician assessment of patient-specific requirements.[15] This emphasis is not merely a legalistic caveat; it reflects the reality that ICU patients present with heterogeneous risk profiles, local microbial ecologies differ substantially, and institutional resources influence diagnostic and treatment pathways. A central principle endorsed by the guideline is the development of local antibiotic programs tailored to individual hospitals, ICUs, regions, or countries.[15] Such programs should be regularly updated and readily accessible to clinicians because microbial prevalence and susceptibility patterns vary markedly across settings. An effective local program should be informed by the organisms most frequently implicated in VAP at that institution and by current antibiogram data, thereby enabling empiric therapy choices that are both likely to be effective and aligned with stewardship goals. The guideline further stresses that antibiotic programs should be evidence-based and shaped by rational prescribing principles that incorporate safety, efficacy, suitability with respect to adverse effect profiles, affordability, and availability, while maintaining a deliberate focus on minimizing the emergence and propagation of resistance.[15] In this way, local programs function as an operational bridge between broad society guidelines and the realities of unit-level microbiology.

For patients with clinically suspected VAP, the guideline recommends empiric antimicrobial therapy with coverage directed toward Staphylococcus aureus, Pseudomonas aeruginosa, and other gram-negative bacilli.[15] This empiric breadth reflects the high prevalence and clinical severity of these pathogens in ICU pneumonia. More intensive empiric antipseudomonal coverage—specifically, combination therapy using two agents from different classes—should be reserved for patients at high risk of resistance, for ICUs where local susceptibility rates are poorly characterized, or where more than 10% of gram-negative isolates demonstrate resistance to monotherapy options.[15] This stratified approach attempts to reconcile the imperative for early effective therapy in high-risk patients with the stewardship need to avoid unnecessarily broad coverage when resistance risk is low. Adjunctive inhaled antimicrobial therapy has also been discussed within VAP management, particularly in scenarios where systemic options are limited. The guideline recommends inhaled antimicrobial therapy as an adjunct to systemic treatment for patients with VAP caused by gram-negative bacilli that are susceptible only to aminoglycosides or polymyxins.[15] In addition, inhaled therapy may be considered for patients who fail to respond to systemic therapy alone, even if concerns exist about the potential for resistance development, because the recommendation prioritizes improved survival outcomes over cost considerations.[15] The rationale for inhaled delivery is to achieve higher local drug concentrations in the airway while potentially limiting systemic toxicity, though implementation requires attention to nebulization technique, ventilator compatibility, and airway secretion management. Regarding treatment duration and stewardship, the recommended course of antimicrobial therapy for VAP is seven days, with the understanding that shorter or longer courses may be warranted depending on clinical trajectory as measured by clinical, radiologic, and laboratory indicators.[15] The guideline also emphasizes de-escalation as a preferred strategy over fixed broad-spectrum regimens. In practice, this means that once culture results and susceptibility profiles are available, clinicians should transition from broad empiric therapy to a narrower regimen targeted at the identified pathogen, which may involve switching antimicrobial agents or reducing combination therapy to monotherapy.[15] Such de-escalation aims to reduce selective pressure for resistance, minimize adverse drug events, and align therapy intensity with demonstrated microbiologic need. Clinical criteria and procalcitonin (PCT) levels may be used to guide discontinuation, though the guideline notes uncertainty regarding whether PCT provides a markedly beneficial incremental signal in this context.[15] The management of immunocompromised patients is additionally acknowledged as requiring a distinct approach due to heightened susceptibility to opportunistic pathogens, even though some general principles—such as timely empiric therapy, attention to local epidemiology, and subsequent tailoring—remain relevant.[15]

The healthcare burden associated with VAP is considerable and extends beyond morbidity and mortality to include substantial resource utilization and cost. In a retrospective analysis of mechanically ventilated participants enrolled in the NASCENT study, the median hospital charges for patients with microbiologically confirmed VAP approached $200,000.[19] The economic impact was accompanied by clinically meaningful consequences, including longer durations of intubation and prolonged hospital stays.[19] These findings reinforce that VAP is not only a clinical complication but also a system-level challenge with implications for ICU bed availability, staffing demands, antimicrobial utilization, and long-term patient recovery trajectories. Collectively, the definitional frameworks, diagnostic limitations, resistant pathogen epidemiology, and stewardship-driven treatment principles outlined in society guidelines provide a structured basis for addressing VAP, yet they also underscore the persistent complexity of managing pneumonia in mechanically ventilated patients.[14][15][16][17][18][19]

Gastrointestinal (GIT) Complications

Gastrointestinal complications occupy a pivotal yet sometimes underappreciated position within the broader landscape of adverse events affecting mechanically ventilated patients. In critical illness, the gastrointestinal tract is not merely a passive organ system susceptible to stress-related injury; it also functions as a dynamic reservoir of microorganisms and inflammatory stimuli that may influence pulmonary infection risk, systemic immune responses, and overall patient outcomes. The close physiological and anatomical relationship between the gastrointestinal tract, the oropharynx, and the lower respiratory system becomes particularly relevant once airway reflexes are blunted, motility is impaired, and an endotracheal tube disrupts normal protective barriers. As a result, the gastrointestinal milieu may contribute to the development of ventilator-associated pneumonia (VAP), bleeding complications, nutritional intolerance, and other clinically significant conditions that complicate weaning and prolong intensive care exposure. Understanding gastrointestinal complications in this setting therefore requires integration of pathophysiologic mechanisms, prophylactic practices, infection prevention priorities, and multidisciplinary care coordination. Mechanically ventilated patients are predisposed to colonization of the stomach by aerobic Gram-negative bacteria (AGNB), a phenomenon that has been repeatedly linked to the pathogenesis of VAP.[20] Several converging factors in critical illness undermine the host's ability to maintain microbial equilibrium within the gastrointestinal tract. Normal clearance of AGNB is impaired, reflecting alterations in gastric acidity, motility, mucosal barrier function, and immune surveillance. In addition, reflux of intestinal contents into the stomach may occur, particularly when gastrointestinal motility is compromised, such as in ileus, which is common among sedated or hemodynamically unstable ICU patients.[20] Refluxed intestinal material often contains bile components, including bilirubin, which can raise gastric pH; this shift is clinically meaningful because a pH greater than 4 provides a favorable environment for gastric AGNB proliferation.[20] Under physiologic conditions, gastric acidity functions as an antimicrobial barrier, limiting bacterial burden and reducing the probability that pathogenic organisms will ascend to the oropharynx or be aspirated. When that barrier is weakened, microbial colonization may expand and become more persistent.

Antimicrobial exposure further modifies this environment in ways that may increase vulnerability to colonization. Patients receiving antibiotics may experience eradication or suppression of normal gastrointestinal flora, thereby weakening colonization resistance and diminishing protective microbial competition.[20] This disruption can facilitate overgrowth of AGNB and, in some contexts, enable fungal proliferation. Certain antibiotic classes—fluoroquinolones are cited as an example—have been associated with promotion of gastric fungal growth, indicating that antimicrobial therapy can reshape the gastric ecosystem in ways that extend beyond bacterial selection pressure.[20] Taken together, reduced clearance, reflux-mediated pH elevation, and microbiome disruption constitute a plausible mechanistic basis for why ventilated patients are at heightened risk for gastric colonization by organisms that may later be implicated in pulmonary infection. The "gastropulmonary hypothesis" offers a conceptual framework linking gastrointestinal colonization to VAP through sequential microbial migration and aspiration.[20] In this model, potentially pathogenic microorganisms may enter the stomach exogenously, such as via contaminated nasogastric feeding tubes, or endogenously through the retrograde movement of intestinal contents into the stomach. Once gastric colonization is established, retrograde colonization of the oropharynx may occur, allowing organisms to occupy upper airway niches in a patient whose normal clearance mechanisms are impaired by sedation, critical illness, and reduced salivary flow. In the presence of an endotracheal tube, repeated microaspiration of colonized oropharyngeal or gastric secretions around the cuff becomes more likely. Over time, these microaspiration events can seed the lower respiratory tract, promote bacterial proliferation, and culminate in VAP.[20] The plausibility of this pathway is reinforced by clinical observations that certain comorbidities, including diabetes mellitus and chronic liver disease, increase the risk of AGNB gastrointestinal colonization.[20] Moreover, colonization tends to appear relatively

early in the ICU course—often within approximately seven days of admission—and appears to correlate with greater disease severity and immunocompromise, suggesting that host vulnerability and physiologic derangement intensify the likelihood of colonization and downstream infection.[20]

In parallel with colonization-related concerns, stress-related mucosal injury and peptic ulceration represent clinically significant gastrointestinal complications in the mechanically ventilated population, particularly because bleeding events can rapidly destabilize critically ill patients. Gastric colonization is described as a factor that predisposes ventilated patients to peptic ulceration and upper gastrointestinal bleeding, making preventive strategies an important component of ICU care, especially among individuals at heightened bleeding risk such as those with coagulopathy.[20] Prophylaxis for stress ulceration has traditionally relied on acid-modifying therapies, with histamine-2 receptor antagonists (H2-RA) and antacids commonly employed. These agents act through different mechanisms—neutralizing existing gastric acid or reducing acid secretion—yet both have demonstrated effectiveness in lowering the risk of ulceration and subsequent upper gastrointestinal bleeding.[20] The clinical dilemma is that these therapies, by design, elevate gastric pH, which may inadvertently facilitate AGNB gastric colonization and thereby increase VAP risk.[20] This trade-off illustrates the challenge of ICU prophylaxis: an intervention beneficial for one high-stakes outcome may amplify risk in another domain. Sucralfate has been discussed as an alternative prophylactic agent because it does not raise gastric pH.[20] Its potential value lies not only in preserving the antimicrobial role of gastric acidity but also in possessing cytoprotective properties that support mucosal defense. Additionally, sucralfate is described as having antimicrobial characteristics that may impede gastric bacterial colonization, aligning with the objective of reducing AGNB proliferation in the stomach.[20] Nonetheless, prophylaxis selection cannot be uniform across all patients. For individuals with elevated risk for severe upper gastrointestinal bleeding, including those with coagulopathy, prophylaxis with an H2-RA rather than sucralfate is recommended, reflecting prioritization of bleeding prevention in those most vulnerable to catastrophic hemorrhagic events.[20] This approach underscores the importance of individualized prophylaxis decisions based on risk stratification, rather than a single prophylactic policy applied indiscriminately. Nutritional strategies have also been examined as potential tools to reduce gastrointestinal complications and, by extension, pulmonary infectious risk. Enteral feeding solutions typically have a pH in the range of six to seven, which may raise gastric pH and thereby promote AGNB colonization when feeds are delivered into the stomach.[20] On this basis, direct delivery of enteral feeds into the small intestine has been proposed as a method to reduce aspiration and pneumonia risk, partly by bypassing the gastric pH-elevating influence of feeds and potentially decreasing gastric residual volumes available for reflux and aspiration.[20] This approach is theoretically attractive because it targets an upstream contributor to colonization and microaspiration. However, evidence supporting the strategy has been inconsistent, and as a result it has not been incorporated into routine standard practice.[20] The lack of routine adoption suggests that practical complexity, variable feasibility, and uncertain outcome benefit have limited its role, despite mechanistic plausibility.

A more direct antimicrobial prevention approach is selective decontamination of the digestive tract (SDD), an intervention designed to counteract impaired colonization resistance in critically ill patients.[20] SDD typically involves administration of three topical, non-absorbable antimicrobial agents—polymyxin E, tobramycin or gentamycin, and amphotericin B—applied to the oropharynx with the intention of suppressing AGNB growth.[20] Delivery into the stomach is facilitated by flushing the agents through a nasogastric or orogastric tube, reflecting the dual focus on upper airway and gastric reservoirs. In addition to topical therapy, SDD incorporates a short systemic antibiotic component, generally a three- to four-day course of an intravenous third-generation cephalosporin at standard doses. This systemic phase aims to provide early coverage for common community-acquired pathogens such as Haemophilus influenzae and Streptococcus pneumoniae, which may contribute to infection early in the ICU stay.[20] Through this combined regimen, SDD seeks to reduce microbial burden in both the oropharyngeal and gastrointestinal compartments during the period of greatest vulnerability. The timing and duration of SDD are operationalized to coincide with ICU exposure and ventilator dependence. The regimen is commonly initiated at ICU admission and discontinued when mechanical ventilation is no longer required or when the patient is discharged from ICU, with duration tailored to individual requirements.[20] Administration is often described as occurring for three days at six-hourly intervals to achieve adequate decontamination, though duration may extend depending on patient needs and institutional protocols.[20] Underpinning this strategy is the concept of colonization resistance, a protective function mediated by normal gastrointestinal flora that limits AGNB colonization through multiple mechanisms. These mechanisms include preventing adherence of AGNB to the gastrointestinal epithelium, facilitating removal of AGNB from the gut, producing toxins that suppress or kill AGNB,

and competing for nutrients in ways that restrict pathogenic growth.[20] Critical illness, antibiotic exposure, and physiologic stress can erode these protective functions, creating a niche for opportunistic colonization; SDD is intended as a structured countermeasure to that erosion.

Evidence has suggested that SDD can reduce the incidence of VAP among ICU patients admitted for medical, surgical, and trauma-related conditions.[20] Furthermore, it has been associated with improvements in outcomes such as reduced mortality, decreased antibiotic requirements, shorter ICU length of stay, and lower healthcare costs in certain contexts.[20] The intervention is described as being especially advantageous in settings where baseline VAP incidence is high and antimicrobial resistance rates are low, a caveat that reflects the delicate balance between infection prevention benefit and the ecological risk of resistance emergence.[20] Despite these reported benefits, SDD has not become a routine standard practice in many institutions. A major concern is the potential for selection of multidrug-resistant organisms, particularly Gram-positive bacteria, as selective pressure alters microbial populations.[20] Additionally, uncertainty persists regarding whether the gastrointestinal tract is indeed the dominant source of the pathogens typically implicated in VAP, raising questions about whether targeting the gut microbiome is the most efficient prevention pathway for all patient populations and ICU environments.[20] The broader clinical significance of gastrointestinal complications becomes especially clear when placed within the structured quality-improvement framework of ventilator bundles, which are widely used to reduce ventilator-associated events (VAEs), including VAP. Hospitals and intensive care units frequently implement bundles that combine several evidence-informed practices into a standardized approach for optimizing care of ventilated patients.[21][22] Although no single ideal bundle exists and bundle composition may vary across hospitals, regions, and countries, core elements tend to be broadly similar because they target shared, modifiable risk pathways. These bundles are designed not only to decrease VAE incidence but also to reduce duration of mechanical ventilation, shorten ICU and hospital length of stay, and reduce mortality.[21][22] Clinical experience has supported the effectiveness of prevention bundles, with notable benefit in reducing VAP occurrence.[21][22] The bundle concept is particularly relevant to gastrointestinal complications because several bundle components directly address reflux, aspiration, stress ulceration, and microbial colonization.

Common bundle elements typically include head-of-bed elevation to approximately 30 to 45 degrees and semi-recumbent positioning, intended to reduce gastric reflux and aspiration and thereby lower VAP risk.[2][21][22] General infection control practices are incorporated to reduce cross-transmission and environmental contamination. Peptic ulcer prophylaxis is included to mitigate bleeding risk, while prophylaxis for deep venous thrombosis addresses another major ICU morbidity domain. Daily spontaneous breathing trials and spontaneous awakening trials, periodic interruption of sedation, and targeted sedation management are intended to accelerate ventilator liberation and reduce cumulative exposure to endotracheal intubation, which is a key driver of VAP risk.[2][21][22] Maintenance of endotracheal cuff pressure within a specified range, often 20 to 30 cm H2O, aims to reduce leakage of colonized secretions around the cuff and limit microaspiration. Subglottic suctioning using closed systems at frequent intervals can remove pooled secretions above the cuff, while oral care with chlorhexidine gluconate targets oropharyngeal microbial burden.[2][21][22] Pressure care is also noted as important, particularly for patients ventilated for prolonged periods or in the prone position, reflecting the need to prevent skin breakdown and associated infection risk.[1] Additional strategies such as early mobilization and conservative fluid management have been described as further measures that may improve outcomes and reduce complications, including those that indirectly influence respiratory and gastrointestinal physiology.[23] High-quality implementation of these prevention and treatment strategies depends fundamentally on team performance and interprofessional collaboration. Surveillance criteria such as those introduced by the CDC in 2013 have functioned as useful performance indicators for mechanically ventilated patients, enabling institutions to monitor VAEs and evaluate quality improvement initiatives.[3] However, surveillance alone does not improve outcomes unless it is paired with effective intervention. The successful deployment of prevention bundles and responsive clinical management requires coordinated expertise across a multidisciplinary team that may include respiratory therapists, nurses, pharmacists, intensivists, critical care physicians, anesthesiologists, and allied health professionals.[24] Each discipline contributes distinct competencies that, when integrated, create a more resilient safety net capable of early detection, rapid response, and consistent preventive care.

Nursing Outcomes:

Nursing practice is central to this ecosystem. Nursing staff commonly operationalize infection control measures, administer prescribed treatments, ensure hydration and nutrition, implement non-pharmacologic therapeutic interventions, provide continuous supportive care, and execute many elements of ventilator bundle protocols in real time.[25][26] These responsibilities are not limited to task completion; they also involve clinical judgment

in recognizing subtle deterioration, anticipating complications, and escalating concerns. Allied health professionals contribute substantially to rehabilitation and recovery, particularly because prolonged ventilation is associated with weakness, delirium, and impaired function. Speech therapy is described as important during weaning processes, reflecting the role of swallowing and airway protection in safe liberation from ventilation and reduction of aspiration risk.[24] Occupational therapy has been reported as safe and beneficial for improving functional outcomes at discharge, reducing delirium duration, and increasing ventilator-free days, highlighting that early rehabilitative intervention can influence not only long-term quality of life but also immediate ICU outcomes.[27] Physiotherapists support mobilization and provide intensive chest physiotherapy, potentially reducing risks such as deep venous thrombosis and extubation failure by improving secretion clearance, muscle conditioning, and cardiopulmonary endurance.[28] Dieticians play a critical role in guiding nutritional support, adapting enteral and parenteral plans to meet metabolic needs while accounting for tolerance, aspiration risk, and evolving clinical status.[29] The importance of communication and coordinated monitoring is particularly pronounced in the context of VAEs because deterioration may begin subtly. A minor clinical change such as new-onset fever can signal the emergence of VAP or progression toward sepsis, and the timeliness of response can influence outcomes.[26] Prompt communication from bedside staff to attending physicians may reduce reaction time to diagnostic and therapeutic intervention, enabling earlier antimicrobial administration when appropriate, earlier source evaluation, and more rapid supportive adjustments. Prevention bundles themselves are most effective when implemented consistently; therefore, monitoring adherence becomes an essential quality function. Patient-centered activities such as structured rounds focused on bundle execution, active correction of deficiencies, ongoing staff education, and engagement of hospital administration and physicians in multidisciplinary prevention initiatives can produce meaningful reductions in VAE rates.[30] This suggests that technical knowledge alone is insufficient; organizational culture, leadership engagement, and continuous improvement processes are also essential determinants of bundle effectiveness.

Ongoing monitoring responsibilities are distributed across the interprofessional team, with nursing staff frequently functioning as the primary continuous surveillance layer. Nurses monitor vital signs, assess clinical stability, identify acute deterioration, and escalate concerns. They work alongside respiratory therapists to monitor ventilator settings and respond to ventilator alarms such as those triggered by acutely decreasing oxygen saturation. They also monitor for decubitus ulcers and other complications, and assess sedation and analgesia needs to support synchrony, safety, and comfort.[26] In addition, monitoring aligned with the CDC VAE surveillance framework is often incorporated to some degree within nursing practice scope, particularly because these criteria rely on physiologic changes and ventilator variables that are routinely assessed.[5] Attending physicians and critical care specialists retain responsibility for diagnosing underlying conditions, instituting holistic management plans, communicating with patients and families, monitoring therapeutic response through clinical, laboratory, and radiologic data, conducting surveillance activities in clinical settings, and maintaining familiarity with current protocols such as local antibiotic programs for empiric management of suspected VAP.[15] Ultimately, interprofessional monitoring, communication, and coordination are shared responsibilities spanning physicians, nurses, respiratory therapists, dieticians, and rehabilitation specialists. This shared accountability is essential for preventing gastrointestinal complications, reducing VAP risk, and optimizing outcomes for mechanically ventilated patients across the continuum of critical care.

Conclusion:

Mechanical ventilation remains indispensable in critical care, yet its associated complications pose serious challenges to patient safety and healthcare systems. VAEs, VILI, and VAP significantly increase morbidity, mortality, and resource utilization. The CDC's surveillance framework provides standardized definitions for monitoring VAEs, but clinical interpretation remains essential to avoid misattribution of causality. Preventing VILI requires individualized ventilator settings, emphasizing low tidal volumes, optimal PEEP, and strategies such as prone positioning and recruitment maneuvers. Adjunctive interventions, including ECMO and neuromuscular blockade, may be necessary in severe cases but carry their own risks. VAP prevention hinges on meticulous airway care, infection control, and adherence to ventilator bundles, which integrate head-of-bed elevation, oral hygiene, sedation protocols, and subglottic suctioning. Nursing professionals are central to these efforts, functioning as the primary surveillance layer and operationalizing preventive measures. Their role extends beyond technical tasks to include early recognition of deterioration, communication with multidisciplinary teams, and patient-centered care. Ultimately, reducing ventilator-related harm requires a coordinated, evidence-based approach that combines surveillance, prevention bundles, and continuous quality improvement. By prioritizing these strategies, healthcare teams can mitigate risks, improve patient outcomes, and optimize resource utilization in high-acuity settings.

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