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The Role of Respiratory Therapists and Nursing In Reducing and Preventing of Ventilator-Associated Pneumonia

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Abstract

Background: Ventilator-associated pneumonia (VAP) comprises ~50% of nosocomial pneumonias and remains the most frequent infection among mechanically ventilated patients, driving mortality, prolonged ICU/hospital length of stay, antimicrobial exposure, and costs. Diagnostic ambiguity, shifting CDC definitions to ventilator-associated events (VAEs), and the SARS-CoV-2 era have complicated surveillance and benchmarking.

Aim: To synthesize practical, evidence-based strategies—especially those enacted by respiratory therapists (RTs) and nursing—to reduce VAP incidence and improve patient-centered outcomes.

Methods: Narrative integration of randomized trials, meta-analyses, and prospective cohorts cited in the source text, emphasizing core bundle elements (head-of-bed elevation, daily sedation interruption, spontaneous breathing trials), early mobilization, oral care/decontamination options, circuit stewardship, subglottic drainage, and implementation science.

Results: Highest-yield measures shorten ventilator exposure and curb aspiration: semirecumbency (30°–45°), light/goal-directed sedation with daily awakening and synchronized SBTs, and early mobilization improve ventilator-free days and functional outcomes. Oral chlorhexidine reduces VAP chiefly in short-stay cardiac cohorts; signals of harm in general ICUs warrant caution. Subglottic drainage lowers early VAP, particularly within comprehensive bundles. Probiotics lack benefit. Compliance, education, and feedback loops determine real-world effectiveness.

Conclusion: RT- and nursing-led, implementation-ready bundles that minimize ventilation days and aspiration—augmented by targeted technologies and antimicrobial stewardship—can meaningfully attenuate VAP while preserving resources.

Keywords: ventilator-associated pneumonia; respiratory therapy; nursing; spontaneous awakening trial.

1. Introduction

Ventilator-associated pneumonia (VAP) represents nearly 50% of all nosocomial pneumonia cases and continues to be the predominant infection in patients requiring invasive mechanical ventilation (Table 1) [1,2]. Its clinical burden has been consistently highlighted across diverse intensive care contexts. The European Prevalence of Infection in Intensive Care (EPIC) III, a large-scale 24-hour point prevalence investigation undertaken on September 13, 2017, in 1150 centers spanning 88 nations, documented that 54% of intensive care unit (ICU) patients had either suspected or microbiologically confirmed infections [3]. Within this cohort, respiratory infections accounted for the majority, comprising 60% of cases, followed by abdominal infections at 18% and bloodstream infections at 15%. Of note, 56% of respiratory infections were either hospital-acquired or ICU-acquired, placing VAP within the broader category of nosocomial respiratory conditions strongly linked to invasive mechanical support [3]. Prior to the emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the consequences of VAP had been well established. It was associated with increased mortality, extended stays both in the ICU and the hospital, excessive and often prolonged antimicrobial utilization, and substantial financial strain on healthcare systems [4,5]. These adverse outcomes collectively justified the prioritization of VAP prevention as a central quality indicator across ICU systems. Consequently, many regulatory agencies and governing organizations promoted structured VAP prevention strategies, frequently incorporating evidence-based bundles and routine surveillance within comprehensive quality improvement frameworks [6].

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Despite considerable focus, debates surrounding the epidemiology and clinical definition of VAP remain unresolved. While advances in microbiological diagnostics—including molecular assays and improved culture techniques—have refined detection and facilitated targeted therapy, challenges persist in distinguishing between tracheobronchial colonization, ventilator-associated tracheobronchitis, and true parenchymal pneumonia. This diagnostic ambiguity contributes to heterogeneous case definitions, variable incidence reporting, and difficulties in comparing outcomes across different ICUs. Even in the presence of improved diagnostic technologies, uncertainty about clinical thresholds and classification has limited standardization efforts, thereby complicating meta-analyses and global epidemiological assessments. The onset of the SARS-CoV-2 pandemic further reshaped the landscape of VAP. ICU systems faced extraordinary patient surges, prolonged durations of ventilation, modifications in sedation and proning practices, and evolving infection-control measures. Additionally, the interplay between viral pneumonitis, bacterial superinfections, and immunomodulatory therapies created a novel clinical context that obscured classical patterns of VAP. Consequently, the effectiveness of conventional prevention bundles and the reliability of outcome data became increasingly difficult to interpret. Many outcome studies during this era have produced inconclusive or conflicting results, reflecting the complex interplay of pandemic-specific confounding variables. These uncertainties highlight the difficulty of evaluating VAP prevention measures within the altered critical-care environment shaped by COVID-19.

In synthesis, VAP continues to represent a major quality and safety concern in modern ICUs. Its prevalence among mechanically ventilated patients [1,2], combined with the predominance of respiratory infections in the ICU [3], underlines the clinical significance of this condition. The established association of VAP with mortality, prolonged hospitalization, and escalated antimicrobial pressure [4,5] reinforces the necessity of sustained preventive interventions and vigilant monitoring. Nonetheless, the definitional inconsistencies and the profound influence of the SARS-CoV-2 pandemic have introduced challenges in surveillance, benchmarking, and data interpretation. Going forward, harmonization of diagnostic criteria, integration of advanced diagnostics, and adaptation of prevention strategies to evolving ICU practices will be essential. Until such consensus is reached, VAP should remain a central focus of ICU quality improvement initiatives [6], while clinicians and researchers critically contextualize epidemiological data in light of the rapidly evolving critical-care environment.

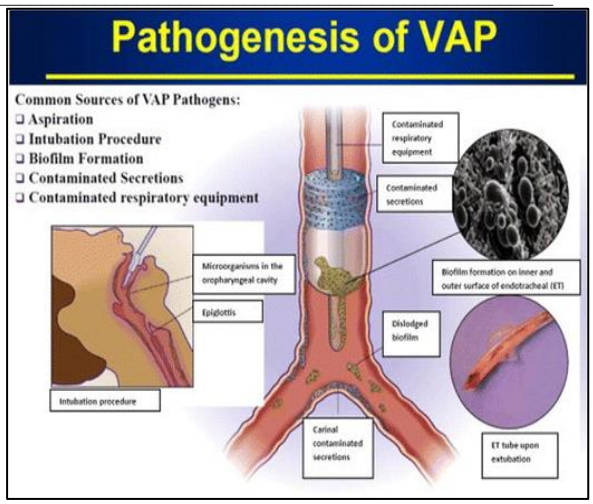

Figure-1: Ventilator-Associated Pneumonia.

Rethinking VAP Definitions, Surveillance, and Prevention:

The earliest Centers for Disease Control and Prevention (CDC) definition of ventilator-associated pneumonia (VAP) placed substantial emphasis on radiographic abnormalities as a cornerstone for diagnosis. Although chest imaging is intuitively appealing for identifying parenchymal infection, reliance on radiographic findings amplified the inherent subjectivity already embedded in bedside symptom appraisal—such as fever, leukocytosis, sputum character, and auscultatory changes—thereby compounding interpretive variability among clinicians and surveillance teams [7,8]. This definitional architecture, vulnerable to interobserver inconsistency and context-dependent thresholds, risked both misclassification and biased trend estimates. Over more than two decades preceding the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, CDC-reported data appeared to demonstrate striking declines in VAP incidence across U.S. hospitals; indeed, some institutions reported the once unimaginable achievement of zero VAP events for prolonged periods [9,10]. Yet, a dissonant clinical reality persisted at the bedside: ICU clinicians continued to diagnose VAP on clinical grounds and to administer targeted antibiotics, pointing to a mismatch between surveillance figures and front-line practice patterns [11,12]. This paradox deepened when placed in an international context, as contemporaneous data from Western Europe and middle-income countries across four continents consistently revealed VAP rates approximately three to five times higher than those reported in the United States, highlighting potential artifacts of surveillance methodology rather than genuine epidemiologic divergence [10, 11, 12].

To reconcile these discrepancies—between U.S. surveillance metrics and global experience, and between administrative rates and clinician-diagnosed disease—the CDC spearheaded a conceptual shift from a VAP-centric case definition toward a broader ventilator-associated events (VAE) framework. The

anchor modifications removed routine radiographic criteria and introduced an objective deterioration in oxygenation occurring after at least 48 hours of prior clinical stability, with the aim of curbing subjectivity while capturing clinically significant ventilator-related complications [13]. In theory, such criteria promised more reproducible surveillance and a tighter coupling to measurable changes in respiratory status. In practice, however, the relationship between VAEs and bona fide VAP proved complex. While it is axiomatic that not all VAEs are pneumonias, accumulating evidence also suggested that not all clinician-recognized VAPs meet VAE thresholds—thereby risking undercounting true infectious episodes when surveillance systems are used as the proxy for clinical incidence [14,15]. This bidirectional mismatch raised foundational questions about using VAE-based indicators to appraise ICU quality related to pneumonia prevention, antimicrobial stewardship, and ventilator management.

Prospective studies of hospital-acquired lung infection reinforced concerns that surveillance definitions may underestimate true disease burden. The PROPHETIC cohort, enrolling adults hospitalized for more than 48 hours and at elevated risk of pneumonia based on exposure to invasive or noninvasive ventilatory support or high supplemental oxygen, found that nearly one-third of patients received treatment for suspected nosocomial pneumonia; of these, more than a third satisfied the study's prespecified pneumonia definition [16]. A complementary investigation in European ICUs (PROPHETIC EU) mirrored these observations, collectively implying that clinical lung infections occur more frequently than U.S. surveillance statistics alone might suggest and that such infections drive a substantial share of antimicrobial use within critical care environments [17]. This gap between treated clinical events and surveilled events is not a mere academic nuance; it shapes the allocation of preventive resources, the calibration of quality metrics, and the credibility of reported gains in infection control. The SARS-CoV-2 pandemic then exerted powerful and multifaceted pressures on this already fragile ecosystem of definitions, surveillance, and prevention. Globally, ICUs were confronted with unprecedented caseloads of patients with severe hypoxemic respiratory failure, prolonged durations of mechanical ventilation, deep and sustained sedation, and frequent proning—conditions that together create fertile ground for ventilator-related complications and secondary bacterial infection. Concomitantly, early diagnostic uncertainty about bacterial coinfection, coupled with the clinical imperative to avoid missing treatable sepsis, fueled widespread empiric antibiotic administration. Within this milieu, rates of VAP and other nosocomial infections surged, as did the selection and emergence of antimicrobial resistance, reshaping the epidemiology of ICU infections within months [18]. Findings from the French REA-REZO surveillance network crystallized these trends in a large comparative cohort: among 64,816 pre-pandemic ICU admissions (2016–2019), 7442 pandemic-era non-COVID-19 admissions, and 1687 pandemic-era COVID-19 positive admissions in 2020, VAP incidences were 14.2%, 18.3%, and 31.9%, respectively; the corresponding attributable mortalities were 3.2%, 2.9%, and 8.1%, revealing a stepwise increase in both frequency and lethality among COVID-19 patients [19]. Parallel U.S. data reported that more than 40% of mechanically ventilated patients with COVID-19 experienced at least one VAP episode, and the probability of infection with antibiotic-resistant organisms escalated with longer ventilator exposure, underscoring the tight linkage between prolonged ventilation, repeated antimicrobial courses, and pathogen ecology [20]. Collectively, the pandemic era reaffirmed that VAP remains a major and dynamic threat in ICUs, particularly when system strain, clinical uncertainty, and extended ventilator dependency converge.

Against this backdrop, diagnostic ambiguity remains the first major challenge for any coherent prevention strategy. If the very act of defining VAP oscillates between radiograph-anchored, symptom-weighted criteria and oxygenation-based, surveillance-oriented thresholds, how should hospitals measure progress and attribute benefits to specific preventive practices? Evidence generated before and during the pandemic indicates that VAP has not vanished from U.S. ICUs; rather, it persists at stable and clinically meaningful rates when scrutinized with patient-level analyses rather than surveillance dashboards. For instance, Medicare reviewers examining randomly selected postsurgical and medical admissions for acute myocardial infarction and congestive heart failure between 2006 and 2010 identified a steady VAP incidence of roughly 10 cases per 100 ventilated patients—an estimate incongruent with claims of near-elimination at the hospital level [21]. Moreover, ventilated hospital-acquired pneumonia (vHAP), a related entity that may not fulfill classic VAP criteria, is both common and associated with higher mortality than VAP, thereby amplifying the cumulative burden of ventilator-era lower respiratory tract infections on patient outcomes and resource utilization [22,23]. These stubborn epidemiologic signals argue for prudence in interpreting surveillance-centered metrics as definitive evidence of success and for renewed emphasis on clinically salient outcomes.

A second, equally consequential layer of complexity arises from the methodological scaffolding that underpins much of the VAP-prevention literature. While randomized, double-blind trials remain the gold standard for isolating causal effects and curtailing observer bias, many influential evaluations of prevention bundles have employed before–after designs. Such time-series approaches, implemented within real-world ICUs, are inherently susceptible to

myriad biases: heightened surveillance intensity following bundle rollout, evolving coding or documentation practices, secular improvements in general critical care, and "Hawthorne effects" wherein awareness of being measured alters behavior. As prevention concepts diffuse and are repeatedly reinforced—akin to the normalization of rapid response teams—ICU cultures evolve, potentially leading to ubiquitous adoption of good practices that extend beyond the explicit bundle elements. Clinicians, sensitized to the risks of VAP, may independently implement adjunctive measures (e.g., minimizing deep sedation, conservative fluid strategies, early mobilization) that confound attribution. Furthermore, contextual heterogeneity—the blend of hospital case mix, ICU type, nurse-to-patient ratios, ventilator management philosophies, and local microbiology—can differentially modulate outcomes, complicating cross-institutional comparisons and meta-analytic synthesis. In short, before–after studies can overstate or understate true effects, and their results must be parsed with attention to confounding, fidelity, and secular drift.

Given the fluidity of definitions and the susceptibility of incidence curves to surveillance artifacts, it is rational to pivot toward more objective and patient-centered outcomes when appraising prevention programs. Yet even VAP-attributable mortality has proven variable across studies, spanning from negligible to substantial effects (0% to 50%), a range that reflects heterogeneity in case mix, diagnostic thresholds, timing and appropriateness of therapy, and competing risks in the critically ill [24,25]. Consequently, composite measures that triangulate the patient experience and resource footprint may better capture the net value of prevention. Mechanical ventilation-free days integrate both survival and liberation from the ventilator; ICU and hospital length of stay index recovery trajectories and downstream bed capacity; and antibiotic exposure quantifies stewardship-relevant ramifications, including selection pressure for resistance and risks of drug toxicity or *Clostridioides difficile* infection. Preventive strategies that reliably improve these outcomes—independent of definitional debate—arguably furnish more compelling evidence of benefit than downward inflections in administratively tallied VAP charts alone. This reframing invites critical reflection on the oft-touted objective of achieving "zero VAP." While zero harm remains an aspirational guiding principle, the biological realities of critical illness, the necessity of invasive ventilation in many cases, and the omnipresence of microaspiration, biofilm formation, and host vulnerability render an absolute zero rate improbable in sustained practice. The notion of zero, frequently coupled to surveillance numbers, risks inadvertently incentivizing documentation artifacts, underreporting, or diagnostic nihilism. A more defensible goal is continuous reduction of preventable events to the lowest achievable level, paired with transparency about definitions, denominators, and data-collection methods. In practical terms, this implies relentless attention to evidence-based care processes—judicious use of noninvasive ventilation when appropriate, daily spontaneous awakening and breathing trials with high fidelity, early mobility for stable patients, consistent head-of-bed elevation when tolerated, parsimonious ventilator circuit manipulation, meticulous hand hygiene and barrier precautions, and tailored consideration of subglottic drainage or specialized endotracheal tubes—while contextualizing any observed incidence shifts within the evolving diagnostic framework.

Importantly, the pandemic experience also underscores the dependencies between prevention and system capacity. Surges that stretch staffing, deplete supplies, and mandate prolonged ventilator days will predictably degrade bundle adherence and compromise infection-control vigilance, tilting the balance toward higher VAP risk. Elevated empiric antibiotic use, although understandable amid diagnostic uncertainty, accelerates selection for resistant organisms, further complicating the clinical course of VAP and raising the bar for effective therapy. These realities should inform preparedness planning: investments in staffing resilience, standardized sedation and ventilator-weaning protocols, rapid diagnostics to de-escalate antibiotics confidently, and antimicrobial stewardship integrated into daily rounds are not luxuries but prerequisites for preventing ventilator-era infections during both routine operations and crisis conditions [18–20]. The REA-REZO gradients in incidence and attributable mortality across pre-pandemic, non-COVID-19 pandemic, and COVID-19 cohorts [19], alongside U.S. observations of rising resistance with ventilator duration [20], illustrate how system stressors and clinical practices co-produce infection risk.

At the same time, surveillance frameworks must evolve to remain clinically meaningful. The VAE construct's emphasis on oxygenation trajectories has advantages for standardization, but its partial overlap with true VAP complicates any performance claims based solely on VAE trends. Hospitals that trumpet falling VAEs as proof of pneumonia prevention may be measuring something broader—or narrower—than intended. Conversely, clinicians diagnosing and treating VAP outside VAE thresholds are signaling that bedside realities still demand individualized judgments that resist neat categorization [14,15]. Bridging this divide calls for hybrid approaches: maintaining VAE surveillance for comparability and signal detection while sustaining clinician-centric audits that review suspected VAP cases, antibiotic decisions, and response to therapy. Layering these data streams with process-of-care measures (e.g., awakening/breathing trial adherence,

head-of-bed elevation compliance, sedation depth) can illuminate where prevention is working and where implementation gaps remain.

The disjunction between surveillance metrics and clinical practice has concrete policy implications. Payment penalties or public reporting tied to surveillance-defined events may inadvertently distort clinician behavior or documentation unless definitions are aligned with clinical judgment and patient-centered outcomes. Furthermore, international benchmarking must adjust for definitional heterogeneity; otherwise, apparent U.S. exceptionalism in low VAP rates may reflect surveillance artifacts more than superior prevention [10, 11, 12]. Research agendas should prioritize prospective, pragmatic trials that test discrete prevention components and bundles against hard endpoints such as ventilator-free days, antibiotic exposure, and mortality—ideally with adjudication frameworks that capture both VAEs and clinician-diagnosed VAP. Mixed-methods evaluations that include implementation of science perspectives can also clarify how culture, staffing, and workflow changes mediate the effectiveness of prevention strategies in diverse ICU settings.

In sum, VAP remains a consequential and persistent complication of mechanical ventilation, not a relic eradicated by surveillance-driven triumphalism. Pre-pandemic reports of near-zero VAP were incongruent with clinician experience and international data; the shift to VAE-based definitions, though motivated by laudable goals of objectivity and reproducibility, only partially maps onto clinical pneumonia and risks underestimating true incidence [7–15]. Prospective cohorts such as PROPHETIC and PROPHETIC EU corroborate a substantial burden of nosocomial lung infection and its central role in antibiotic consumption in critically ill populations [16,17]. The pandemic crystallized these lessons by dramatically elevating VAP risk and resistance pressures in ventilated patients, particularly those with COVID-19, with measurable increases in both incidence and attributable mortality [18–20]. Meanwhile, carefully conducted reviews continue to find stable, clinically significant VAP rates in U.S. ICUs when individual patient data, rather than surveillance abstractions, are examined [21], and related entities such as ventilated hospital-acquired pneumonia carry even greater mortality, magnifying the stakes for prevention and early, appropriate therapy [22,23]. Moving forward, prevention programs should be judged less by fluctuating incidence curves and more by improvements in objective, patient-centered outcomes—mechanical ventilation-free days, lengths of stay, and antimicrobial utilization—while acknowledging that VAP-attributable mortality estimates will vary with context and case mix [24,25]. Hospitals should resist the seductive but unrealistic promise of sustained "zero VAP" and instead pursue asymptotic reduction through rigorous, high-fidelity implementation of proven practices, adaptive learning when local data reveal gaps, and honest accounting of definitions and denominators. Ultimately, redefining success in VAP prevention requires aligning surveillance with clinical reality, strengthening the evidentiary base with robust, pragmatic trials, and building resilient ICU systems capable of maintaining prevention excellence under both ordinary and extraordinary pressures.

Table 1. Core RT/Nursing Bundle Elements and Evidence Signals

Element	Primary RT/Nursing Actions	Mechanism Targeted	Evidence signals from text	Expected Impact
Head-of-bed elevation 30°–45°	Maintain/verify angle; contraindication checks; use visual cues/devices	Reduces reflux and microaspiration	RCT and reviews show lower VAP; adherence challenges; no benefit to lateral Trendelenburg; prone not protective [33–41]	↓ VAP risk; facilitates mobilization/extubation
Daily sedation interruption (SAT) & light sedation	Daily safety screens; minimize benzodiazepines; prefer dexmedetomidine when appropriate; document targets	Shortens ventilation, improves arousability	Trials/meta-analyses: −2–4 days ventilation; ↑ ventilator-free days; mortality signal favorable in bundles [38,42–47]	↑ VFDs; ↓ ICU/hospital LOS
Spontaneous breathing trials (SBTs)	Daily readiness checks; RT-driven protocols; T-piece or low PS acceptable	Accelerates ventilator liberation	RCTs/meta-analyses: ↓ MV duration/LOS/cost; compliance often low [47–52]	↑ VFDs; ↓ exposure-time for VAP
Early mobilization	Progressive PT/OT; hemodynamic/safety screens	Counters deconditioning/delirium; improves mechanics	Safe in high-risk groups; adds VFDs and functional gains [53–55]	↑ VFDs; ↓ delirium; ↑ function
Circuit stewardship	Avoid unnecessary disconnections and suction	Limits exogenous inoculation	Safe; no consistent direct VAP reduction; plausibly reduces contamination [60–61]	Process reliability; ↓ contamination risk

Potential strategies and role of respiratory therapists in ventilator-associated pneumonia prevention:

Ventilator-associated pneumonia (VAP) is best understood as a syndrome rather than a single nosologic entity, arising in heterogeneous intensive

care unit (ICU) populations with diverse antecedent illnesses, surgical exposures, and trajectories of critical illness. This heterogeneity begets variability in incidence across units and patient cohorts, reflecting differences in baseline host vulnerability, the intensity and duration of ventilatory support, and the microbiological ecology in which patients are embedded. The etiologic profile of VAP—and, by extension, the contours of empiric and targeted antibacterial therapy—is shaped not only by immutable host factors such as immunocompetence and prior colonization, but also by modifiable care-process variables including days of mechanical ventilation, elapsed hospitalization before pneumonia onset, and the local prevalence of antimicrobial resistance within the institution's microbiome. These considerations carry practical implications for prevention: high-cost devices and specialized interventions should be preferentially directed toward patients or units with the greatest risk, such as those with prolonged ventilation or care environments characterized by elevated rates of multidrug-resistant organisms, whereas universally applicable, high-value measures ought to be deployed broadly to all at-risk patients, calibrated to the resources and implementation capacity of the local ICU. A pragmatic, tiered strategy—aligning prevention intensity with patient- and unit-level risk—offers a plausible path to maximize benefit while stewarding scarce resources, even if such tailoring can sometimes complicate frontline acceptance and uniformity of practice among health care providers [26,27].

Over the past two decades, multiple care elements have been studied individually and in combination as components of ventilator bundles, with the most effective frameworks explicitly acknowledging the dual pathogenesis of VAP: first, colonization of the aerodigestive tract by potential pathogens; and second, aspiration of contaminated secretions into the lower respiratory tract. Bundle design that simultaneously interrupts both pathways—limiting acquisition and overgrowth of pathogenic flora while reducing the likelihood and volume of aspiration—has consistently produced the most credible reductions in VAP risk. Among the determinants of VAP, however, the duration of invasive ventilation stands out as both a biologically intuitive and empirically robust driver of infection risk, as well as a contributor to the selection of resistant organisms under the pressure of sustained antibiotic exposure [20]. Consequently, prevention begins upstream: averting intubation when safe alternatives exist, employing noninvasive support judiciously, and once intubated, executing high-fidelity strategies that hasten liberation from the ventilator. By compressing the window during which microaspiration, biofilm formation, and colonization can occur, such approaches reduce both infection probability and the cumulative opportunity for resistance to emerge.

Equally salient is the tempo at which hospitalized patients, particularly those in the ICU, acquire nosocomial flora. Colonization by hospital-adapted microbes can develop within 48 hours of admission, a kinetic reality that should inform both empiric therapy choices and the architecture of preventive measures. In practice, this mandates granular awareness of unit-specific antibiograms, resistance trends, and sentinel organisms, so that prevention programs target the pathogens most likely to produce clinically meaningful harm in the local environment. Patient-level risk stratification further refines this focus: immunosuppression, recent hospitalizations, prior antibiotic exposures, and admission from nursing homes or long-term acute care facilities are well-established enhancers of the risk that VAP will be caused by antibiotic-resistant bacteria [28,29]. These infections disproportionately threaten outcomes, largely by increasing the chances of initially ineffective antibiotic therapy—a scenario consistently linked to worse morbidity and mortality. Thus, while VAP prevention should be universal in principle, the marginal gains from intensified, higher-cost interventions will be greatest in populations where resistant pathogens are most prevalent and where delays to appropriate therapy would exact the highest toll.

Aspiration biology forms the third pillar of rational prevention. The pathophysiologic pipeline—contaminated secretions in the oropharynx or stomach, reflux into the pharynx, and subsequent passage through or around the endotracheal tube—represents both a dominant causal pathway and a highly preventable target for intervention. Elegant radiolabeling studies have demonstrated the traversal of gastric contents from the stomach to the airways via the pharynx in supine, mechanically ventilated patients, making visible the stealthy microaspiration that often escapes clinical detection [30]. Complementary investigations reveal the commonplace aspiration of bacterial-laden oral secretions into the bronchial tree, underlining the mouth and oropharynx as persistent reservoirs for pathogen inoculation of the lower respiratory tract [31,32]. These mechanistic insights translate directly into actionable prevention priorities: minimize conditions that promote reflux and pooling of secretions; maintain head-of-bed elevation when hemodynamically tolerable; reduce endotracheal tube leakage past the cuff; and ensure meticulous oral hygiene that suppresses bacterial load in the upper aerodigestive tract. Each of these interventions narrows the conduit by which colonization is converted into infection.

Synthesizing these strands, a coherent prevention paradigm emerges that is simultaneously population-aware, process-driven, and ecology-

informed. At the population level, ICUs should operationalize tiered risk stratification that flags patients at heightened likelihood of resistant VAP—those with profound immune suppression, recent or recurrent hospitalizations, extended prior antibiotic courses, or transfer from facilities with weaker infection-control infrastructures—for augmented precautions and enhanced surveillance [28,29]. At the process level, prevention bundles should prioritize interventions with the strongest evidence for reducing ventilation days: consistent spontaneous awakening and breathing trials, thoughtful sedation and analgesia titration to avoid unnecessary deep sedation, and early mobilization when feasible. These practices not only shorten exposure to the ventilator but also counteract deconditioning and delirium, accelerating readiness for extubation. Adjunctive measures that directly mitigate aspiration—routine head-of-bed elevation, subglottic secretion management where appropriate, and conservative handling of ventilator circuits to avoid unnecessary breaks—should be standardized with auditing for adherence, recognizing that their effect sizes often depend on implementation fidelity and integration with the broader bundle.

Microbiological stewardship is the necessary companion to these process measures. Because colonization dynamics accelerate soon after ICU admission, preventive efforts that diminish the density and virulence of oropharyngeal flora, coupled with stringent hand hygiene and contact precautions, can meaningfully lower the probability that any single aspiration event will seed clinically significant infection. Crucially, stewardship also extends to antibiotic prescribing: avoiding indiscriminate empiricism and embracing timely de-escalation when diagnostic data permit reduces selective pressure for resistance, thereby lowering downstream VAP severity and complexity. This stewardship lens should inform decisions about deploying higher-cost devices—such as specialized endotracheal tubes or continuous subglottic suction—reserving them for settings and patients in which the local risk-benefit calculus is favorable, such as units with persistently elevated VAP rates driven by resistant organisms. Such targeting aligns resource intensity with anticipated benefit, a principle essential for sustainability in constrained health systems [26,27].

Implementation of science perspectives are indispensable for translating these strategies from guidelines into durable practice. The most elegant prevention bundle will founder if daily workflows do not support reliable execution, if staffing ratios and skill mix are misaligned with protocol demands, or if unit culture fails to prioritize prevention behaviors. Education and feedback loops, real-time prompts embedded in electronic records, and interdisciplinary rounds that explicitly review extubation readiness, sedation depth, and aspiration precautions can raise adherence from theoretical to routine. Measuring what matters—ventilator-free days, antibiotic exposure, and length of stay—keeps teams focused on outcomes less susceptible to definitional drift, while still tracking VAP incidence with transparent criteria for local quality improvement. When barriers arise, thoughtful adaptation that preserves core intervention intent while accommodating local constraints will outperform rigid, top-down mandate. Finally, prevention programs must remain adaptive to the shifting epidemiology of critical illness. Surges in ICU demand, evolving ventilatory strategies, and the changing landscape of antimicrobial resistance can all alter the relative yield of individual prevention components. The principle of continuous learning—frequent data review, targeted PDSA (plan–do–study–act) cycles, and willingness to reallocate resources when the evidence or local ecology changes—ensures that VAP prevention remains dynamic rather than dogmatic. In this learning health system approach, zero harm is embraced as an aspirational compass, while realism about biological and operational constraints guides the incremental pursuit of "as low as reasonably achievable" infection risk.

In conclusion, effective VAP prevention requires an integrated strategy that addresses the syndrome's heterogeneity, the centrality of ventilator exposure, and the primacy of aspiration as a mechanistic driver. High-value, broadly applicable measures should form the foundation for all ventilated patients, while more costly or labor-intensive interventions are reserved for those at heightened risk or for units with entrenched problems linked to resistant pathogens [26,27]. Recognizing that prolonged mechanical ventilation potentiates both infection risk and resistance pressure underscores the primacy of early liberation from the ventilator as a unifying objective [20]. Equally, a sober appreciation of rapid colonization dynamics and patient-level risk factors—immunosuppression, prior hospitalizations, antecedent antibiotic use, and residence in facilities with variable infection control—sharpens the focus on those VAP episodes most likely to harm patients and challenge therapy [28,29]. Mechanistic evidence tracing the path of contaminated gastric and oral secretions into the airways, particularly in supine, intubated patients, crystallizes aspiration as the modifiable fulcrum for prevention [30,31,32]. By aligning population risk, process reliability, and ecological stewardship within a flexible implementation framework, ICUs can meaningfully attenuate the burden of VAP while deploying resources judiciously and preserving the therapeutic armamentarium for the patients who need it most.

Practical approaches to ventilator-associated pneumonia prevention

Designing a pragmatic, durable ventilator-associated pneumonia (VAP) prevention bundle begins with identifying those "non-negotiable" measures that are most consistently linked to reductions in VAP and, ideally, to improvements in harder, patient-centered outcomes such as ventilator-

free days, length of stay, and mortality. Ease of application and favorable cost profiles are valuable attributes, but they are not sufficient on their own; prevention programs must also be resilient to shifting case mix, variable staffing skill sets, evolving local microbiology, and the shocks posed by pandemics or supply chain disruptions. With these contextual realities in view, secondary elements can be layered onto the foundational bundle according to institutional resources and priorities, being careful to avoid accretion of low-yield components that inflate workload, fragment attention, and erode compliance. In this domain, restraint is often strategic: doing fewer things exquisitely well typically outperforms doing many things inconsistently, particularly when the added interventions lack robust links to objective outcomes. Among the core measures, head-of-bed elevation, conscientious minimization of sedation through daily awakening, and systematic spontaneous breathing trials (SBTs) have the most coherent mechanistic rationale and the strongest practice-enabling evidence base. Each speaks directly to the principal levers that convert colonization into infection: the physics of aspiration, the time under invasive ventilation during which microaspiration, biofilm accrual, and bacterial overgrowth can occur, and the organizational capacity to execute daily liberation checks. The following synthesis integrates the salient evidence and operational lessons for these pillars, emphasizing how they can be embedded, audited, and sustained within a contemporary ICU.

Head-of-bed elevation to the semirecumbent range (approximately 30°–45°) remains one of the oldest, most intuitive, and most implementable measures to mitigate aspiration. The physiological rationale is grounded in decades of observation that supine positioning facilitates gastroesophageal reflux and pooling of oropharyngeal secretions, thereby increasing the probability that contaminated material will traverse the glottis or leak around the endotracheal tube (ETT) cuff into the lower airways [30]. While it is theoretically possible that semirecumbency might, through gravity, promote more rapid descent of secretions once they cross the larynx, the dominant effect appears protective: in a randomized trial of 86 mechanically ventilated patients, the semirecumbent posture produced approximately a fourfold reduction in both clinically suspected and microbiologically confirmed nosocomial pneumonia compared with flat positioning [33]. Translation to routine practice, however, has long been hampered by inconsistent adherence. Early observational cohorts documented disappointingly low compliance with sustained elevation targets, highlighting the gap between evidence and execution [34]. Subsequent quality-improvement efforts have demonstrated that simple, low-friction nudges—visual cues at the bedside, integrated angle indicators, and small devices affixed to rails—can anchor attention and improve adherence across shifts [35,36]. When the totality of evidence is pooled, the picture remains cautiously favorable: a Cochrane review, limited by small trials and risk of bias, nonetheless found an overall reduction in VAP when patients were positioned between 30° and 60° versus 0° to 10°, although the effect did not translate into a statistically significant reduction in microbiologically confirmed VAP in the available dataset [37]. This pattern—signal toward benefit on syndrome-level outcomes with attenuated effect on culture-confirmed events—is consonant with the multifactorial nature of VAP and the imperfect sensitivity of diagnostic thresholds.

Attempts to optimize posture beyond semirecumbency have been less persuasive. In a large multicenter trial contrasting semirecumbent positioning with the lateral Trendelenburg posture, overall VAP incidence was very low (0.5%), and although the lateral Trendelenburg arm showed fewer microbiologically confirmed cases, neither primary nor secondary endpoints achieved statistical significance; more importantly, the lateral Trendelenburg strategy incurred a higher burden of serious adverse events, including vomiting, intracranial hemorrhage, and brachial plexus injury, rendering it unsuitable for bundle inclusion on safety grounds [39]. Prone positioning, notwithstanding its established role in severe hypoxemia, has not shown convincing reductions in VAP incidence in dedicated trials, further underscoring that posture alone is not a panacea [40]. In pragmatic terms, semirecumbency remains the safest, simplest, and most scalable posture for hemodynamically stable ventilated patients, with ancillary benefits for mobilization and extubation readiness; where available, endotracheal tubes with subglottic suction ports can offset any residual gravitational disadvantage by continuously evacuating pooled secretions above the cuff [41].

If gravity and anatomy determine whether aspirated material reaches the lung, time on the ventilator determines how often that opportunity arises. Consequently, sedation management that accelerates awakening and extubation is a linchpin of prevention. Daily awakening trials—structured interruptions of continuous sedatives with careful safety screening—have repeatedly been associated with shorter mechanical ventilation by roughly two to four days, a magnitude of effect that is large enough to plausibly translate into fewer VAP episodes through simple exposure reduction [42]. The principle has matured from a provocative intervention to standard of care, with guideline endorsement and widespread protocolization. Nuance remains in how best to operationalize light sedation as a default: a Danish trial suggested that an “analgesia-first” approach—prioritizing pain control without routine sedatives—can similarly shorten ventilation, although the absolute ventilation times in both arms exceeded those in the classic trial by Kress and colleagues, reflecting context

and practice differences that influence generalizability [43]. Combining awakening with synchronized SBTs appears to compound benefits. In a multicenter trial of 336 patients, coupling daily sedation interruption with daily breathing trials produced more ventilator-free days (14.7 vs 11.6), as well as faster ICU and hospital discharge, underscoring the value of integrating these checks into a single, disciplined daily ritual [44]. Observational analyses reinforce these advantages: in a study dissecting the relative contributions of bundle components, daily sedation interruption emerged among the strongest predictors of earlier extubation, shorter hospital stay, and even reduced ventilator mortality [38]. Not all contexts replicate these findings exactly. A multicenter Canadian trial in 16 hospitals, where benzodiazepines were the predominant sedatives, found no difference in intubation duration between a nursing-driven light-sedation protocol and daily interruptions; importantly, the interruption arm received higher cumulative daily sedative doses and boluses than in prior work, which may have blunted benefits and illustrates how pharmacologic choices and dosing paradigms shape outcomes [45]. The pragmatic conclusion endures defaulting to light, goal-directed sedation, with routine daily awakening when safe, is a foundational tactic for preventing prolonged ventilation and the VAP that tracks with it.

Implementation data clarify which practices make daily awakening and SBTs more likely to occur. In a recent analysis across multiple U.S. centers, factors independently associated with higher odds of performing next-day spontaneous awakening and breathing trials included the use of physical restraints, documentation of target sedation levels, more frequent arousal assessments, and administration of dexmedetomidine—features that collectively signal a culture of explicit sedation management and the choice of sedatives that facilitate arousability [46]. By contrast, deep sedation or coma, and the use of benzodiazepines or ketamine, independently predicted lower odds of conducting these trials, consistent with extensive literature linking heavier sedation to protracted ventilation [46]. When ICU bundles explicitly include spontaneous awakening trials (SATs) within their core, meta-analytic syntheses report downstream benefits that extend beyond VAP surrogates: shorter ICU stays, reduced time on the ventilator, decreased delirium, and lower ICU and hospital mortality, as well as earlier mobilization—an outcome that itself loops back to promote liberation [47]. For these reasons, awakening strategies and avoidance of excess sedation should be treated not as mere adjuncts but as essential architecture in any VAP prevention plan. The logic of daily SBTs is similarly straightforward: frequent, standardized assessment of readiness to breathe with minimal assistance enables clinicians to identify and act upon the earliest safe moment for extubation. Across randomized and quasi-randomized trials, readiness assessments and SBTs consistently shorten mechanical ventilation, trim ICU length of stay, and reduce hospitalization costs, with effects that have proven robust enough to justify widespread protocolization and integration into ventilator order sets [47,48]. Once codified, these practices become more “automatic,” reducing reliance on individual clinician memory and counteracting decision inertia [49,50]. Heterogeneous meta-analyses that combine different trial designs converge on the same conclusion: routine SBTs are associated with earlier liberation and improved resource utilization [51]. In many ICUs, SATs and SBTs are now yoked in a synchronized daily cadence—awakening to test cognition and respiratory drive, followed immediately by a breathing trial where indicated—which simplifies team choreography and concentrates the clinical work into a predictable window.

Despite consensus on efficacy, adherence to daily SBTs often lags behind other bundle elements, a pattern repeatedly observed in implementation studies. In the same analysis that highlighted the potency of daily sedation interruption, breathing trials ranked among the lowest in compliance, a sobering reminder that the most effective interventions are not always the easiest to deliver consistently in busy, unpredictable ICUs [38]. The measured impacts of SBTs on surveillance-defined outcomes also require careful interpretation. While SBTs clearly reduce ventilator days and have been associated with fewer ventilator-associated events (VAEs), their effects on “possible VAP” rates have been inconsistent, with one analysis showing no statistically significant difference (odds ratio 0.7; 95% CI 0.4–1.6; P=.5) [38]. This discrepancy likely reflects definitional boundaries rather than biological futility: fewer days on a ventilator must, by arithmetic, shrink the window during which VAP can occur, even if surveillance categories fail to capture all clinically treated events. Crucially, the choice of SBT modality—T-piece trials versus low-level pressure support—does not seem to influence rates of pneumonia or other key outcomes, reinforcing that the essential act is to perform SBTs reliably, not to fixate on the technical variant [52]. From a systems perspective, embedding prompts in electronic records, scheduling SBTs into daily huddles, and empowering respiratory therapists with protocolized autonomy can lift compliance and translate trial efficacy into real-world effectiveness.

Bringing these elements together, a high-functioning VAP prevention bundle has a few defining characteristics. First, it codifies semirecumbent positioning as the default for all hemodynamically stable ventilated patients, with explicit contraindications and a mechanism to revisit the angle at set intervals. Second, it normalizes light, analgesia-first sedation, incorporates daily awakening with a clear safety checklist, and pairs SATs with SBTs in a synchronized routine that all disciplines recognize and support. Third, it measures and feeds back performance not only on VAP incidence (with transparent definitions) but on ventilator-free days,

sedation targets achieved, percentage of eligible days with SATs/SBTs completed, and extubation timing after passing trials. Finally, it respects the reality that prevention happens in a complex adaptive system: workload, staffing, patient acuity, and external shocks will ebb and flow. As a result, the bundle should be resilient—simple enough to survive the night shift and surge weeks, yet rigorous enough to change trajectories when executed with fidelity.

Two corollaries flow from this approach. The first is that adjunctive technologies should be selected judiciously. Endotracheal tubes equipped with subglottic suction may be prioritized in units with stubborn VAP rates or in patient subsets expected to require prolonged ventilation, particularly since they complement semirecumbency by removing pooled secretions that gravity alone cannot manage [41]. Conversely, strategies such as lateral Trendelenburg positioning, despite theoretical benefits in secretion drainage, pose unacceptable safety risks and have not demonstrated convincing outcome advantages, and therefore should be eschewed [39]. The second corollary is that culture matters as much as components. Units that routinely document a target sedation level for every patient, assess arousal frequently, and default to sedatives like dexmedetomidine that facilitate wakefulness create conditions in which SATs and SBTs are the path of least resistance; the inverse is true where deep benzodiazepine sedation remains the norm [46]. Leaders can cultivate this culture by aligning protocols, order sets, and performance dashboards with liberation-first priorities, and by celebrating process reliability as a clinical achievement on par with more dramatic interventions.

In conclusion, practical prevention of ventilator-associated pneumonia is less about discovering new, exotic interventions and more about relentlessly executing a small number of high-yield practices that shorten ventilator exposure and blunt aspiration risk. Head-of-bed elevation to 30°–45° in stable patients, reinforced through unobtrusive compliance aids, reduces aspiration-mediated inoculation and supports mobilization [30,33–37]. Daily awakening, anchored in light, goal-directed sedation, compresses ventilation time and amplifies the impact of synchronized SBTs, with reproducible gains in ventilator-free days, lengths of stay, and even survival in bundle-based implementations [38,42–47]. Systematic SBTs—agnostic to whether they use a T-piece or pressure support—translate readiness into earlier extubation when performed reliably, even if their effects are more evident in ventilator-exposure metrics than in surveillance-defined VAP categories [47–52]. A prevention bundle built on these elements, audited with meaningful patient-centered metrics, and adapted to local constraints will not eradicate VAP, but it will make VAP rarer, briefer, and less deadly—precisely the kind of progress that matters most at the bedside.

Early mobilization, hand hygiene, ventilator circuit stewardship, and adjunctive measures

Early mobilization has emerged as a cornerstone of contemporary critical care and a pragmatic, high-yield tactic within ventilator-associated pneumonia (VAP) prevention programs. Building on the insight that prolonged immobility perpetuates diaphragmatic weakness, global deconditioning, delirium, and ventilator dependence, structured physical therapy in the ICU has been shown to be feasible and safe even in patients traditionally perceived as “too sick to mobilize,” including those with acute respiratory distress syndrome, on continuous renal replacement therapy, receiving vasopressors for shock, or living with obesity (body mass index >30) [53]. Safety screens, task-specific protocols, and interprofessional choreography enable mobility across a spectrum of acuity, and the signal on outcomes is consistent: when implemented early and systematically, mobilization shortens the duration of invasive mechanical ventilation. Importantly, the benefits of mobility appear additive to those derived from daily sedation interruption. In cohorts already utilizing spontaneous awakening as standard practice, the superimposition of early mobilization yielded additional gains in ventilator-free days (23.5 vs 21.1, P = .05), suggesting complementary mechanisms: awakening restores cognition and respiratory drive, while mobilization counters disuse, enhances ventilatory mechanics, and accelerates readiness for extubation [54]. A programmatic approach to whole-body rehabilitation—interweaving early sedation minimization with physical and occupational therapy in the opening days of critical illness—has also been shown to be safe and well tolerated, translating into better functional status at discharge, fewer days spent in delirium, and more ventilator-free days compared with usual care [55]. These findings argue that mobility should not be viewed as an optional add-on but as a core process tightly linked to VAP prevention via the shared pathway of reducing ventilator exposure.

Parallel to mobility, meticulous attention to infection prevention fundamentals—particularly hand hygiene—remains indispensable for curbing the transmission of nosocomial pathogens that later seed VAP. Both soap-and-water handwashing and alcohol-based hand rubs have repeatedly been associated with lower rates of cross-transmission and nosocomial infections. The face validity of hand hygiene is matched by encouraging quasi-experimental data: in an interrupted time-series study, a slimmed-down “ventilator bundle” comprising only hand hygiene, chlorhexidine oral care, and targeted education of health care personnel was associated with a 59% reduction in VAP rates [56]. Yet, a paradox endures. Despite its simplicity and ubiquity, hand hygiene is

frequently the weakest link in bundle adherence, with compliance reported as low as 10% to 15% in some settings, a deficit that reflects workflow pressures, human factors, and competing priorities at the bedside [57]. Use of gowns and gloves when caring for patients colonized or infected with highly resistant organisms can further attenuate transmission of multidrug-resistant pathogens, but here too the magnitude of effect is modulated by the fidelity of implementation and local ecology. When the totality of evidence is weighed, enhanced hand hygiene likely contributes to VAP prevention, though the strength of inference is limited by the quality and heterogeneity of supporting studies and by the difficulty of isolating hand hygiene's effect from concurrent interventions in complex ICUs [58,59]. Pragmatically, hospitals should couple education with environmental redesign (e.g., ubiquitous sanitizer placement), real-time feedback, and leadership reinforcement to transform compliance from aspiration to habit.

Another practical domain is ventilator circuit stewardship, which emphasizes minimizing needless circuit disconnections and avoiding unnecessary manipulation. The theoretical rationale is straightforward: each break in the closed system creates an opportunity for bacteria to enter the lower airway, while circuit stability preserves humidification and reduces fluctuations in airway pressures. Evidence indicates that maintaining the integrity of ventilator circuits is safe and can reduce bacterial ingress into the trachea, even though trials have not consistently demonstrated a direct impact on VAP incidence [60,61]. In a similar vein, avoiding routine, non-indicated endotracheal suctioning reduces the risk of introducing pathogens and causing mucosal trauma, thereby removing one more conduit by which colonization can convert to infection. The take-home message is that "do no harm" applies equally to devices: unnecessary handling can tip the balance toward contamination, whereas restraint preserves the protective value of closed systems. Beyond these foundational practices lie adjunctive strategies targeting aspiration, microaspiration, and the bacterial burden above and around the endotracheal tube (ETT). One of the most intensively studied approaches is subglottic secretion drainage via specialized ETTs that permit evacuation of pooled secretions that collect above the cuff. By lowering the volume and bacterial density of material available for seepage into the lower airways, these tubes aim to blunt the initiating event of many VAPs. Across randomized trials and several meta-analyses, subglottic drainage has been associated with an approximately 50% reduction in early-onset VAP, although heterogeneity in pneumonia definitions, expected ventilation durations, and suctioning methods (continuous versus intermittent) complicates direct comparisons [62,63,64]. The earliest synthesis by Dezfulian and colleagues, pooling five randomized trials, suggested not only lower VAP but also shorter durations of mechanical ventilation and ICU stay with subglottic drainage [62]. A subsequent, larger meta-analysis by Muscedere et al. (13 trials; 2442 patients) partially reproduced these findings but flagged substantial heterogeneity that biased analyses of ventilation time and length of stay [63]. In contrast, a later review by Caroff and colleagues, incorporating four newer trials, did not confirm shorter ventilation or overall stay benefits; exclusion of a single outlier study from China reinforced this neutral finding on these secondary endpoints while preserving the signal for VAP reduction [64,65]. More recently, the greatest reductions in VAP have been reported when subglottic suctioning is embedded within a comprehensive ICU care bundle that includes the Institute for Healthcare Improvement's ventilator elements and vigilant ETT cuff pressure management, yielding >50% decreases in VAP—an effect that underscores the synergy of aligned processes rather than reliance on a single technology [66].

ETT cuff pressure itself is a critical variable at the interface between colonized secretions and the distal airway. Best practice targets a cuff pressure of 25–30 cm H2O to create an effective seal that reduces leakage while minimizing tracheal mucosal ischemia. Investigations comparing intermittent versus continuous cuff pressure monitoring—whether via pneumatic or electronic devices—have produced conflicting results on aspiration rates, tracheal secretion volumes, bacterial loads, and VAP incidence [67,68,69]. A pragmatic trial comparing two manual monitoring strategies found that more frequent checks did not translate into discernible clinical advantages, including VAP reduction [70]. Likewise, a large study in trauma patients showed that automated continuous regulation with a pneumatic device failed to outperform routine care in preventing VAP [71]. These mixed results suggest that while maintaining cuff pressures within the recommended range is important, how that end is achieved may be less consequential than ensuring consistent, reliable practice by the care team.

Re-engineering the cuff or the tube material has also been proposed as a way to block microaspiration channels. Tapered cuffs and polyurethane materials—designed to reduce folds and microchannels—performed inconsistently in animal work and small human studies, and in two randomized trials did not deliver measurable reductions in VAP [72,73]. A French multicenter trial in 326 patients across 10 ICUs examined whether tapered cuffs reduced microaspiration of gastric contents, measured by pepsin and salivary amylase in tracheal aspirates; outcomes, including microaspiration rates and pneumonia incidence, were similar between groups, although the tapered cuff arm exhibited less tracheobronchial bacterial colonization [74]. It is noteworthy that prior work found tracheal salivary amylase to only moderately correlate with microaspiration (AUROC 0.56), which may limit the

sensitivity of the chosen biomarker [75]. Even so, the most recent meta-analysis synthesizing six randomized trials again failed to show a VAP reduction with tapered cuffs in critically ill and postoperative populations [76]. These converging data temper enthusiasm for cuff redesign as a standalone prevention lever.

Antimicrobial surface technology offers a different angle of attack. In a large randomized trial, silver-coated ETTs produced a 36% relative risk reduction in microbiologically confirmed VAP, suggesting that anti-biofilm properties can meaningfully alter the clinical trajectory [77]. Whether these tubes are cost-effective in routine practice remains uncertain, particularly in ICUs where baseline VAP incidence is already low; the acquisition costs may not be offset by avoided infections in such contexts [78,79]. Moreover, a small study testing periodic intraluminal cleaning of silver-coated tubes with an endOclear catheter failed to reduce colonization of either the tube or the lower respiratory tract compared with standard suctioning, casting doubt on the additive value of mechanical cleaning adjuncts—especially in standard (non-silver) ETTs where robust clinical trials are lacking [80]. On balance, silver-coated tubes appear promising for select high-risk populations or units with stubborn VAP rates, but universal adoption is difficult to justify without clearer cost-benefit data. Gastrointestinal factors intersect with aspiration risk in mechanistically direct ways. Gastric overdistention promotes gastroesophageal reflux and augments both micro- and macroaspiration events. While naso- or orogastric tubes are standard for enteral feeding and decompression, routine monitoring of gastric residual volumes is no longer recommended after a large, randomized trial demonstrated no benefit to this practice and raised concerns about unnecessary feeding interruptions [81]. Where feasible, orogastric tubes are preferred over nasogastric tubes to reduce nosocomial sinusitis, a potential upstream reservoir for lower airway seeding [82]. The message here is not to abandon enteral nutrition but to deliver it thoughtfully, avoiding practices that amplify reflux without providing commensurate safety.

Selective digestive decontamination (SDD) and selective oral decontamination (SOD) remain among the most debated adjuncts in VAP prevention. In European ICUs characterized by low background resistance and lower antibiotic consumption, SDD has been promulgated as a core element of prevention guidelines, notably in France [83]. SDD typically combines a topical regimen—oral paste and gastric suspension of colistin, tobramycin, and nystatin throughout mechanical ventilation—with a four-day course of a broad-spectrum intravenous antibiotic, often a third-generation cephalosporin. Studies from these settings have associated SDD with reductions in VAP and, in some analyses, in mortality and other hard outcomes [84,85,86]. A large Dutch cluster-randomized crossover trial involving nearly 6000 ICU patients compared SDD with SOD and standard care; although the initial report required retraction and revision due to misclassification of intervention periods at one ICU, subsequent syntheses have generally supported clinical benefit in low-resistance environments [85]. A meta-analysis pooling 32 trials and 24,389 patients concluded that SDD, relative to standard care or placebo, was associated with lower hospital mortality, though the certainty of evidence regarding impacts on antimicrobial resistance was very low, reflecting heterogeneity and limitations in ecological surveillance [87]. Notably, a more recent Australian randomized trial of SDD versus placebo in 5982 mechanically ventilated patients did not find a mortality difference (27.0% vs 29.1%; mean difference −1.7%; 95% CI −4.8%–1.3%), tempering generalized claims of survival benefit outside the specific European contexts in which earlier gains were observed [88].

The crux of the SDD/SOD debate is antimicrobial ecology. The routine use of third-generation cephalosporins as part of SDD raises legitimate concerns about selection for methicillin-resistant *Staphylococcus aureus* (MRSA), extended-spectrum β-lactamase (ESBL)-producing Enterobacteriaceae, and *Pseudomonas aeruginosa*—patterns of resistance that often emerge after antibiotic exposure and were amplified during the SARS-CoV-2 pandemic as empiric use escalated [20]. Some prior studies reported no increase in aminoglycoside or colistin resistance at SDD/SOD sites, and in certain large trials there was even a decrease in colonization with resistant strains and lower overall resistance to third-generation cephalosporins, suggesting that ecological effects may be context-dependent and, at least transiently, favorable in low-resistance settings [89,90,91,92]. Transient upticks in susceptible *S. aureus* and *Enterococcus faecalis* at the initiation of SDD were described but reportedly abated after about five years of use, indicating possible ecological adaptation over time [93]. Conversely, work by Oostdijk and colleagues examining ecological effects in all ICU patients—not just those receiving SDD/SOD—found that rectal and respiratory colonization with ceftazidime-resistant strains more than doubled after the end of the SDD period following an initial decline during active SDD implementation (from 5% to 15%, P = .05 for the trend in respiratory samples), raising alarms about rebound phenomena when programs are discontinued [94]. Additional nuance comes from a Dutch cohort (2011–2015) of ventilated patients receiving SDD, in which rectal colonization by Gram-negative bacteria correlated with ICU-acquired infections (over half in the respiratory tract), but congruence between rectal and respiratory species was only 35%, complicating simplistic causal narratives that gastrointestinal flora

invariably drive VAP [95]. Ultimately, heterogeneity in local ecology, stewardship capacity, and background resistance pressures makes "one size fits all" recommendations untenable.

Given this complexity, a calibrated stance has emerged from European guidance: consider SOD—but not SDD—in ICUs where antimicrobial resistance rates are low (<5%) and antibiotic consumption is modest (<1000 daily doses per 1000 admission days) [96]. This position recognizes that most rigorous SDD trials derive from northern European units with favorable ecologies, and that external validity may be limited in regions with moderate-to-high resistance burdens. Even proponents of SDD acknowledge in narrative reviews that where resistance prevalence is low, SDD is consistently associated with less resistance and improved outcomes, whereas in settings with higher baseline resistance the benefits on clinically meaningful endpoints remain unproven and must be weighed against ecological risks [97]. For hospitals outside the low-resistance archetype, the practical implication is to prioritize universally applicable, high-value measures (e.g., mobilization, sedation minimization, aspiration precautions, hand hygiene) and to reserve ecology-sensitive interventions like SDD/SOD for carefully selected contexts with robust stewardship and surveillance infrastructures.

Taken together, a pragmatic VAP prevention program knits these elements into an integrated, implementation-ready fabric. Early mobilization—interlocked with daily awakening and synchronized spontaneous breathing trials—shrinks time on the ventilator and reduces the opportunity for aspiration-driven infection [53–55]. Hand hygiene and contact precautions curb the propagation of resistant organisms within the unit, acknowledging that compliance is the rate-limiting step and must be actively engineered through design and feedback [56–59]. Ventilator circuit stewardship preserves the integrity of the airway interface, limiting exogenous contamination and avoiding unnecessary suctioning that can inoculate the bronchial tree [60,61]. Adjunctive technologies—subglottic drainage, careful cuff-pressure management, judicious selection of ETT materials or coatings—offer incremental gains when chosen and implemented wisely, especially as part of comprehensive bundles and in populations with prolonged ventilation [62–77]. Nutritional practices that avoid gastric overdistention and favor orogastric tubes when indicated reduce upstream drivers of reflux and sinusitis [81,82]. Finally, ecology-modifying strategies such as SOD and SDD should be deployed, if at all, in settings where the resistance landscape and stewardship resources render benefits plausible and risks manageable, with eyes wide open to the possibility of unintended ecological consequences and the need for ongoing surveillance [83–97]. This layered, context-aware approach does not promise the elimination of VAP; rather, it offers a credible pathway to make VAP rarer, briefer, and less injurious—precisely the outcomes that matter most to patients and clinicians alike.

Optimizing oral care has long been viewed as a logical cornerstone of ventilator-associated pneumonia (VAP) prevention because aspiration of oropharyngeal secretions is a principal pathway by which pathogens access the lower respiratory tract. Accordingly, a wide range of oral decontamination strategies has been evaluated, spanning simple mechanical plaque control (tooth brushing with toothpaste), antiseptic rinses or gels (most commonly chlorhexidine and povidone–iodine), and topical antibiotic approaches such as selective oral decontamination (SOD). The aggregate evidence for tooth brushing alone is modest. Across four trials, routine brushing did not yield measurable reductions in VAP incidence or improvements in other hard outcomes, tempering expectations that mechanical plaque removal, by itself, can meaningfully disrupt the aspiration–infection cascade in critically ill, intubated patients [98]. A more recent systematic review screened 2337 records and ultimately synthesized a small subset—four studies in the qualitative review, three in the meta-analysis—comparing combined tooth brushing plus chlorhexidine against chlorhexidine alone. Investigators concluded that sample sizes were too small and trial quality too variable to support definitive judgments, calling for larger, methodologically rigorous studies to clarify any incremental benefit of adding brushing to antiseptic care [99]. Still, because tooth brushing is low cost, low risk, and straightforward to implement, it remains reasonable as a routine component of oral hygiene in mechanically ventilated patients, particularly when integrated into broader prevention bundles that address aspiration risk and sedation minimization.

Antiseptic oral care entered ICU practice on strong biologic plausibility and encouraging early data. Initial randomized trials in cardiac surgery cohorts—patients with short, predictable intubations and relatively homogeneous risk—suggested that chlorhexidine could reduce VAP and, in some analyses, mortality [100]. As evidence accumulated across settings and populations, subsequent meta-analyses painted a more nuanced picture. Povidone–iodine appeared to confer less benefit than chlorhexidine, and the principal signal for both seemed to be fewer VAP events rather than consistent improvements in mortality, ventilator duration, or ICU length of stay [101,102,103]. In recent years, the net clinical value of chlorhexidine has been re-examined with more granularity. A network meta-analysis from the United Kingdom—focused specifically on mortality—reported an increased risk of death associated with chlorhexidine in general ICU populations (odds ratio [OR] 1.25, 95% CI 1.05–1.5) [104]. In the same analysis, SDD emerged as the most favorable intervention with respect to mortality (OR

0.73, 95% CI 0.64–0.84), with SOD also demonstrating benefit (OR 0.85, 95% CI 0.74–0.97) [104]. A detailed meta-analysis by Klompas and colleagues further disentangled population effects: the apparent 27% reduction in VAP attributed to chlorhexidine was driven largely by cardiac surgery trials, whereas for noncardiac ICU patients the confidence interval crossed unity (OR 0.78, 95% CI 0.6–1.02), and there was a concerning, albeit not statistically significant, trend toward higher mortality (risk ratio 1.13, 95% CI 0.99–1.29) [105]. When bundle components were analyzed separately, the same group identified a stronger association between chlorhexidine use and ventilator mortality (hazard ratio 1.6, 95% CI 1.2–2.3, P = .06), further fueling debate about routine use across heterogeneous ICU populations [38]. Reflecting these uncertainties, European Respiratory Society guidelines favored SOD but declined to recommend chlorhexidine for VAP prevention, emphasizing the need to match interventions to the populations most likely to benefit while avoiding potential harm [96].

Two contemporary meta-analyses have nonetheless concluded that oral chlorhexidine is associated with reduced VAP rates without a statistically demonstrable mortality penalty, but both qualify their conclusions by noting that the underlying evidence is low quality, heterogeneous, and underpowered to define optimal dosing or concentration strategies [106,107]. In practical terms, this evolving evidence base suggests a cautious, context-sensitive approach: chlorhexidine may remain reasonable in narrowly defined groups (e.g., short-stay, postsurgical patients with brief expected ventilation) while broader, routine use in general medical ICU populations merits reappraisal, particularly in the presence of alternative strategies with stronger outcome associations. Systemic antibiotic prophylaxis represents a more aggressive strategy predicated on the observation that aspiration of bacterially contaminated secretions—especially in patients with impaired airway reflexes—drives early-onset nosocomial pneumonia. Evidence to date is limited and focused on selecting high-risk cohorts. A meta-analysis that identified three studies encompassing 267 largely comatose patients after head trauma found that short-course intravenous antibiotics were associated with lower VAP incidence and shorter ICU stays but did not reduce mortality or mechanical ventilation duration [108]. Extending this concept to a contemporary postcardiac arrest population treated with targeted temperature management (32–34 °C), a recent randomized trial of nearly 200 participants demonstrated that a two-day course of amoxicillin–clavulanate reduced VAP risk without improving other key end points such as ventilator-free days or 28-day mortality [109]. These findings illustrate the trade-offs inherent in prophylaxis: a narrower, time-limited systemic regimen can suppress early infectious events in precisely defined contexts of aspiration risk, but it has not translated into broader outcome gains, and it raises stewardship questions about selection pressure. As such, routine adoption in unselected ICU populations is not supported; instead, prophylaxis may be reserved for carefully screened, short-horizon scenarios in which aspiration risk is both high and transient.

Microbiome-modulating interventions, most notably probiotics, have also been investigated as potential VAP countermeasures. Earlier syntheses linked probiotic administration to improved VAP rates, but without measurable effects on mortality, ventilation duration, or ICU/hospital length of stay, implying that any microbiologic benefits did not cascade into system-level outcome improvements [110,111]. More recently, a large randomized controlled trial enrolling 2650 mechanically ventilated patients tested *Lactobacillus rhamnosus* GG against placebo and found no significant difference in VAP development, effectively neutralizing prior optimism and leading to a consensus statement against routine probiotic use in critically ill adults for the purpose of VAP prevention [112]. Safety considerations—including the rare but consequential risk of probiotic-associated bacteremia in profoundly immunocompromised hosts—further support a restrained stance absent compelling efficacy signals.

Beyond the selection of specific interventions, bundle compliance and the human factors that drive it are decisive determinants of real-world effectiveness. Publishing a list of recommended elements is insufficient; sustainable gains require engaged, informed, and empowered teams, robust audit-and-feedback systems, and continuous education that adapts to turnover and evolving practice. In general, higher bundle adherence correlates with better outcomes, yet even low compliance has occasionally coincided with improved VAP rates, reflecting the complexity of causal pathways and the possibility that certain “keystone” elements exert outsized influence [57]. Importantly, provider understanding of VAP pathophysiology and prevention correlates with improved adherence, highlighting education as both a process measure and an implementation lever [113]. The most dramatic, durable reductions in VAP have typically followed a staged rollout of mandatory measures, with full effect manifesting only after 12–24 months—an implementation horizon that underscores the need for patience, reinforcement, and iterative refinement [114]. Compliance is not monolithic: some components (e.g., head-of-bed elevation) achieve high, sustained adherence, whereas others (e.g., daily SBTs) lag without targeted workflow engineering [57,113]. It is also realistic to expect diminishing returns: even well-designed programs encounter a “floor effect,” beyond which VAP incidence resists further reduction despite

additional effort, likely reflecting irreducible biological and operational constraints [115].

Recent observational data complicate the presumed linear relationship between compliance and outcomes. One academic center reported that ventilator bundle compliance did not associate with lower risks of ventilator-associated events (VAEs) or VAP; notably, higher adherence to chlorhexidine oral care correlated with increased VAE risk, a finding that may reflect confounding by indication, surveillance artifacts, or unmeasured practice patterns [116]. Conversely, a trauma ICU study documented short-term VAP reduction after implementing a standardized, evidence-based prevention protocol, aligning with the more traditional narrative that disciplined bundle execution yields tangible benefits [117]. Looking ahead, emerging artificial intelligence (AI) methods may help bridge the gap between population-level bundles and patient-specific risk by flagging individuals at high short-term probability of VAP, enabling targeted intensification of prevention measures and more efficient resource allocation [118,119]. For now, the pragmatic lesson is to measure processes and outcomes transparently, interrogate outliers, and be prepared to recalibrate bundles as new evidence and local data dictate.

The economics of VAP prevention are increasingly salient in an era of constrained resources and competing priorities. Cost-effectiveness is dynamic: unit prices evolve, staffing models shift, and baseline VAP incidence may decline as standard care improves, all of which can recalibrate the value proposition of specific measures. A thoughtful analysis by Branch-Elliman and colleagues evaluated strategies from both hospital and societal perspectives, concluding that, for hospitals, the Institute for Healthcare Improvement (IHI) ventilator bundle, subglottic suctioning, and probiotics represented preferred options, whereas from a societal vantage point, chlorhexidine oral care and selective digestive decontamination (SDD) emerged as favorable [78]. These findings should be interpreted with caution in light of more recent data challenging routine probiotics and raising questions about chlorhexidine in general ICU populations [105,112]. Moreover, cost-effectiveness is context-dependent: it varies by ICU type (e.g., trauma vs cardiothoracic), case mix, local resistance ecology, and the degree to which an intervention influences long-term outcomes such as antimicrobial resistance. A contemporary systematic review found that effective bundle implementation was associated with both clinical and economic advantages but emphasized that study heterogeneity—differences in bundle composition, definitions, comparators, and costing methods—limited the strength of conclusions about absolute savings and the relative ranking of components [120]. The prudent approach is therefore twofold: first, prioritize universally high-value, low-cost, low-harm interventions with reproducible links to reduced ventilator exposure and aspiration (e.g., daily awakening and SBTs, head-of-bed elevation, mobility, hand hygiene, ventilator circuit stewardship); second, deploy costlier or ecology-sensitive modalities (e.g., subglottic suction tubes, SOD/SDD) selectively in settings where local epidemiology and implementation capacity predict net benefit, accompanied by active surveillance for unintended consequences.

Bringing these strands together, a modern oral-care–centered strategy for VAP prevention should be embedded within a broader, multipronged framework that minimizes time on the ventilator, reduces the density and virulence of colonizing flora, and disrupts the mechanical pathways of aspiration. Tooth brushing remains good practice for general hygiene but cannot be expected to lower VAP on its own [98,99]. Chlorhexidine's role appears limited and population-specific: it may reduce VAP among short-stay cardiac surgical patients yet lacks convincing mortality benefit, and general ICU use demands caution in light of signals for harm in some analyses [100–107]. SOD and SDD carry stronger outcome signals in select low-resistance environments but bring stewardship complexities that preclude blanket recommendations; if considered, they should be nested within rigorous antimicrobial governance and ecological monitoring [96]. Prophylactic systemic antibiotics can reduce early VAP in tightly defined, high-aspiration-risk scenarios but have not consistently improved broader outcomes and should not be generalized indiscriminately [108,109]. Probiotics, once promising, failed to demonstrate benefit in the largest, best-conducted trial and are not recommended for routine prevention [110–112]. Above all, success hinges on people and systems: engaged clinicians, reliable workflows, continuous measurement, and a culture that treats prevention as everyday craftsmanship rather than episodic campaign. In practice, this means standardizing oral care with explicit protocols (including frequency, agent, and contraindications); aligning sedation and mobility pathways so that patients are awake and participating in therapy as early as possible; maintaining semirecumbency; protecting the integrity of the ventilator circuit; and using subglottic drainage and other device-level adjuncts where the risk-benefit ratio is favorable. It also means acknowledging uncertainty, watching the local data, and adjusting course—tightening or relaxing specific components—as evidence and ecology evolve. The endpoint is not theoretical perfection but the steady reduction of preventable lung infections, fewer antibiotic days, shorter ventilations, better functional recovery, and more patients leaving the ICU alive and independent. Such outcomes, rather than any single intervention's allure, should anchor decisions about what belongs in a VAP prevention bundle and how oral decontamination fits within it.

Table 2. Oral Care/Decontamination Modalities: Effects and Caveats

Modality	Typical ICU Use	Effect on VAP	Effect on Mortality/Other Outcomes	Key Caveats/Notes
Tooth brushing ± toothpaste	Twice daily with suction	No reduction vs control across four studies [98]; uncertain incremental benefit when added to chlorhexidine [99]	Insufficient evidence for LOS/MV changes	Low-cost/low-risk; reasonable hygiene practice
Chlorhexidine (CHX) oral care	0.12–2% swab/gel	↓ VAP largely in cardiac surgery cohorts [100–105]	Signals of ↑ mortality in general ICUs in network/meta-analyses; uncertain optimal dose [104–107]	Consider selectively; avoid blanket use in general ICUs
Povidone–iodine	Antiseptic alternative	Less benefit than CHX [101–103]	No consistent outcome gains	Limited role
Selective oral decontamination (SOD)	Topical colistin/tobramycin/nystatin	Mortality/VAP benefits in some settings [104,85]	Benefits context-dependent	Favorable in low-resistance ICUs; stewardship required
Probiotics	Enteral probiotic courses	No benefit in largest RCT [112]	No improvement; potential safety concerns	Not recommended for routine prevention

Conclusion:

Ventilator-associated pneumonia persists as a consequential, preventable complication of invasive ventilation. Across diverse ICU settings, the most reliable path to risk reduction is not a single technology but a coherent, RT- and nursing-driven bundle that (1) compresses time on the ventilator and (2) disrupts aspiration pathways. Semirecumbent positioning, daily sedation interruption with light, analgesia-first strategies, and synchronized spontaneous breathing trials synergistically hasten liberation from the ventilator while lowering opportunity for microaspiration. Early mobilization safely adds ventilator-free days and functional gains, even in "high-risk" cohorts. Device-level adjuncts—most notably subglottic drainage—provide incremental benefit when embedded within disciplined care processes; by contrast, routine probiotics are unsupported, and the role of oral chlorhexidine appears population-specific, warranting caution in general medical ICUs. Because definitions and surveillance constructs (e.g., VAEs) incompletely capture clinical VAP, programs should be judged by patient-centered outcomes—ventilator-free days, lengths of stay, and antimicrobial utilization—rather than incidence curves alone. Ultimately, durable success depends on implementation: clear protocols, bedside checklists, real-time audit/feedback, and continuous education to maintain high compliance amidst staffing variability and surges. Layered with antimicrobial stewardship and awareness of local resistance ecology, this pragmatic blueprint makes VAP rarer, briefer, and less injurious, achieving clinically meaningful benefit without imposing unsustainable burdens on teams or resources.

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