Supplementary Information File

Summary table of diagnostic criteria for Ventilator Associated Pneumonia (VAP) recommended in national and international guidelines

Guideline & reference	Method	Clinical Features	Radiological Features	Microbiological Features	Other
United Kingdom Guidelines R. G. Masterton, A. Galloway, G. French, M. Street, J. Armstrong, E. Brown, J. Cleverley, P. Dilworth, C. Fry, A. D. Gascoigne, A. Knox, D. Nathwani, R. Spencer, M. Wilcox, (2008) Guidelines for the management of hospital-acquired pneumonia in the UK: Report of the Working Party on Hospital-Acquired Pneumonia of the British Society for Antimicrobial Chemotherapy, Journal of Antimicrobial Chemotherapy, Volume 62, Issue 1, Pages 5–34, https://doi.org/10.1093/jac/dkn162	• Working Party of the British Society of Antimicrobial Chemotherapy (BSAC). • A systematic review approach using a formally evaluated quality assessment mechanism. • The tool chosen was the guideline development process produced by the Scottish Intercollegiate Guideline Network (SIGN).	• Fever (core temperature > 38.8°C) • Blood leucocytosis or leucopoenia (<4000 or >1000 leucocytes/mm^3) • Purulent tracheal secretions • Increased oxygen requirement	• A good quality CXR should be obtained and compared with previous CXRs if available. • Clinical criteria with the presence of a new and/or persistent infiltrate on chest radiograph (CXR), which is otherwise unexplained. • CT scanning may assist in the differential diagnosis of HAP and may guide management in patients who are not responding to treatment and who have a complex CXR.	• The results of microbiological investigations should guide the causal pathogens and their therapy. • Not all organisms isolated from respiratory specimens in individual patients should be regarded as pathogens that necessarily require therapy; they should be interpreted and treated in the light of the full clinical picture, if necessary, after consultation between microbiologists and clinicians. • We recommend that the least expensive, least invasive, and most rapid sampling technique requiring minimal expertise be used to establish a microbiological diagnosis. • Quantitative cultures should not be relied on.	• VAP is usually defined as pneumonia developing ≥48 h after implementing ET intubation and/or mechanical ventilation that was not present before intubation • Lung biopsy/ histology is not recommended. • The CPIS may help select patients for short-course therapy and monitor response to treatment.
American Guidelines American Thoracic Society; Infectious Diseases Society of America (2005) Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-	• The ATS/IDSA Guideline Committee • Each individual was assigned a topic for review and presentation to the entire group. The committee	• To exclude other sources, all patients must have a comprehensive medical history and undergo a physical examination.	• Chest radiograph, with new or progressive infiltrates. A posteroanterior and lateral CXR if possible, to identify the severity and identify other sources/ complications.	• Samples of lower respiratory tract secretions should be obtained from all patients with suspected VAP, and should be collected before antibiotic changes.	• Mechanically ventilated for more than 48 hours • All patients should have blood cultures, to identify sources. • Delays in the initiation of appropriate antibiotic therapy can increase the mortality of

associated pneumonia. Am J Respir Crit Care Med; 15;171(4):388-416. doi: 10.1164/rccm.200405-644ST. PMID: 15699079.	discussed the data and formulated recommendations. • All available and relevant, peer-reviewed studies published until July 2004 were considered. • A grading system for the evidence-based recommendations was used; high-level (Level I), moderate-level (Level II), and low-level (Level III) evidence.	• Fever (body temperature increase of greater than 1°C or greater than 38.3°C) • Leucocytosis (25% increase and a value greater than 10.0 × 10^9/L) or leukopenia (25% decrease and a value less than 5.0 × 10^9/L) • Purulent tracheal secretions, alongside clinical signs of infection. (greater than 25 neutrophils per high power field) • Arterial oxygen saturations and blood gases, along with other laboratory results, to define the severity of illness.	• For patients with ARDS, for whom it is difficult to demonstrate the deterioration of radiographic images, at least one of the three clinical criteria or other signs of pneumonia should lead to more diagnostic tests.	• Samples can include an endotracheal aspirate, bronchoalveolar lavage sample, or protected specimen brush sample. • Semiquantitative cultures of tracheal aspirates cannot be used as reliably as quantitative cultures. • If bronchoscopic sampling is not immediately available, non-bronchoscopic sampling can reliably obtain lower respiratory tract secretions for quantitative cultures, which can be used to guide antibiotic therapy decisions.	VAP, and thus therapy should not be postponed to perform diagnostic studies in clinically unstable patients • If there is a high probability of pneumonia, prompt therapy is required, regardless of whether bacteria are found on microscopic examination of lower respiratory tract samples.
American Guidelines Kalil AC, Metersky ML, Klompas M, et al. (2016) Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clin Infect Dis. 2016 Sep 1;63(5):e61-e111. doi: 10.1093/cid/ciw353. Epub 2016 Jul 14. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4981759/pdf/ciw353.pdf	• ATS and the IDSA collaboration to create updated guidelines for diagnosing and treating HAP and VAP. • A total of 18 subject-matter experts comprised the full panel, which included specialists in infectious diseases, pulmonary medicine, critical care medicine, laboratory medicine, microbiology, and pharmacology, as well as a guideline methodologist • Searches were limited to studies performed in adults and those published in English or containing an English abstract. No publication year limits were used. To	• Not discussed	• Not discussed	• Cultures of respiratory secretions should be obtained from virtually all patients with suspected VAP • Non-invasive sampling with semiquantitative cultures is used to diagnose VAP, rather than invasive sampling with quantitative cultures and non-invasive sampling with quantitative cultures. Non-invasive respiratory sampling refers to endotracheal aspiration. • However, the panel recognises that some clinicians occasionally perform invasive quantitative cultures. For patients with suspected VAP whose invasive quantitative	• Clinical factors should also be considered because they may alter whether to withhold or continue antibiotics. These include the likelihood of an alternative source of infection, prior antimicrobial therapy at the time of culture, degree of clinical suspicion, signs of severe sepsis, and evidence of clinical improvement. • For patients with suspected HAP/VAP, we recommend using clinical criteria alone rather than using biomarkers (CRP, sTREM-1, PCT) • For patients with suspected HAP/VAP, we suggest using clinical criteria alone rather than using CPIS plus clinical

	supplement the electronic searches, panellists contacted experts and hand-searched journals, conference proceedings, reference lists, and regulatory agency websites for relevant articles as needed. • Evidence summaries for each question were prepared by the panel members using the GRADE approach for rating the confidence in the evidence			culture results are below the diagnostic threshold for VAP, we suggest that antibiotics be withheld rather than continued	criteria to decide whether or not to initiate antibiotic therapy • Blood cultures for all patients with suspected VAP are recommended.
Canadian Guidelines Rotstein C, Evans G, Born A, Grossman R, Light RB, Magder S, McTaggart B, Weiss K, Zhanel GG. Clinical practice guidelines for hospital-acquired pneumonia and ventilator-associated pneumonia in adults. Can J Infect Dis Med Microbiol. 2008 Jan;19(1):19-53. doi: 10.1155/2008/593289.	• The Association of Medical Microbiology and Infectious Disease Canada and the Canadian Thoracic Society, • Group members represented the areas of infectious diseases, respirology, critical care and pharmacy. • A standard grading system was used to classify each recommendation according to its strength (A–E) and the quality of the evidence • Each member of the group was assigned a subject for review. • For each subject, a literature search was undertaken of English-language peer-reviewed papers and abstracts until December 2006, using relevant key words pertinent to that subject.	• At least two of the following three findings: fever, leukocytosis and purulent tracheal secretions, along with abnormal findings from chest radiographic studies • In the absence of such findings, no further investigations are required and observation will suffice. • If the patient has two or more features, a CXR should be ordered. • Temperature greater than 38°C or less than 36°C • Leucopenia or leucocytosis • Purulent tracheal secretions • Decreased PaO_2	The presence of a radiographic infiltrate in a patient with fever, leukocytosis or purulent tracheobronchial secretions The diagnosis of VAP is based on chest radiography findings of; • Alveolar infiltrates • Air bronchograms • New or worsened infiltrates	It is recommended that for most patients a clinical approach supplemented by non-invasive quantitative cultures of respiratory tract samples is sufficient to guide appropriate antibiotic choices. Invasive diagnostic testing has not been demonstrated to improve clinical outcomes and therefore is not recommended unless dealing with immunocompromised hosts.	The CPIS score should be calculated to improve sensitivity and specificity for the diagnosis of VAP. In the case of ventilated patients, if the CPIS is between 4 and 6, pneumonia should be considered if no alternative diagnosis for the findings can be obtained because of the mortality associated with this disease. Therapy should be considered taking into account the Gram stain of tracheobronchial secretions. If the CPIS is greater than 6, a Gram stain of tracheobronchial secretions should be obtained and cultures of the secretions undertaken. Treatment should be started based on the findings of the Gram stain and

	• Information was sorted and tabulated. All documents were merged, and a working draft was prepared for review by all members. The completed document was reviewed and approved by the aforementioned societies.				consideration of local epidemiology. The CPIS should be recalculated daily and cessation of antibiotics should be considered if the CPIS remains below 6 by day 3. Treatment should be based on the results of diagnostic testing. Decisions about empirical therapy should be determined by the patient's clinical stability, risk factors for resistant pathogens and the local epidemiology, together with the results of preliminary tests.
European Guidelines European Centre for Disease Prevention and Control. European surveillance of healthcare- associated infections in intensive care units (2015) https://www.ecdc.europa.eu/sites/default/files/media/en/publications/Publications/healthcare-associated-infections-HAI-ICU-protocol.pdf AND Hospitals in Europe Link for Infection Control through Surveillance (HELICS) (2004) Surveillance of Nosocomial	ECDC: This document is based on version 6.1 of the HELICS-ICU protocol issued in September 2004. Changes to the protocol have been applied, either based on agreements made during the annual meetings of the European network for the surveillance of healthcare-associated infections (HAI-Net) in June 2009 and June 2010, or because they were necessary for the integration of the HAI surveillance data HELICS: The consensus for the new protocol is based on; An in-depth analysis of the methodology of existing	CXR changes and at least one of the following; • Fever > 38 °C with no other cause • Leukopenia (< 4 000 WBC/mm^3) or leucocytosis (≥ 12 000 WBC/mm^3). And at least one of the following; • New onset of purulent sputum, or change in character of sputum (colour, odour, quantity, consistency) • Cough or dyspnea or tachypnea • Suggestive auscultation (rales or bronchial breath sounds), rhonchi, wheezing • Worsening gas exchange (e.g. O_2 desaturation or increased	Two or more serial chest X-rays or CT-scans with a suggestive image of pneumonia for patients with underlying cardiac or pulmonary disease. In patients without underlying cardiac or pulmonary disease, one definitive chest X-ray or CT-scan is sufficient. In addition to clinical symptoms as listed.	a) Bacteriologic diagnostic performed by: Positive quantitative culture from minimally contaminated LRT specimen • Bronchoalveolar lavage (BAL) with a threshold of ≥ 10^4 colony forming units (CFU)/ml or ≥ 5% of BAL-obtained cells contain intracellular bacteria on direct microscopic exam (classified on the diagnostic category BAL) • Protected brush (PB Wimberley) with a threshold of ≥ 10^3 CFU/ml • Distal protected aspirate (DPA) with a threshold of ≥ 10^3 CFU/ml.	X-ray, clinical symptoms and microbiology features needed in combination – not as standalone features.

Infections in Intensive Care Units Protocol Version 6.1 https://www.sicsag.scot.nhs.uk/hai/helics_protocol.pdf	national/regopma; surveillance networks, and a questionnaire sent out to HELICS-ICU Working Party members designed to measure opinions for the new protocol. Several meetings of the steering group took place to integrate into the protocol. Both guidelines state identical diagnostic criteria	oxygen requirements or increased ventilation demand).		Positive quantitative culture from possibly contaminated LRT specimen • Quantitative culture of LRT specimen (e.g. endotracheal aspirate) with a threshold of 10^6 CFU/ml. b) Alternative microbiology methods; • Positive blood culture not related to another source of infection • Positive growth in culture of pleural fluid • Pleural or pulmonary abscess with positive needle aspiration • Histologic pulmonary exam shows evidence of pneumonia • Positive exams for pneumonia with virus or particular germs (Legionella, Aspergillus, mycobacteria, mycoplasma, Pneumocystis carinii): - Positive detection of viral antigen or antibody from respiratory secretions (e.g. EIA, FAMA, shell vial assay, PCR) - Positive direct exam or positive culture from bronchial secretions or tissue - Seroconversion (example: influenza viruses, Legionella, Chlamydia) - Detection of antigens in urine (Legionella). c) Others	

				• Positive sputum culture or non-quantitative LRT specimen culture • No positive microbiology	
International Guidelines Guidelines for the management of hospital-acquired pneumonia (HAP)/ ventilator-associated pneumonia (VAP) of the European Respiratory Society (ERS), European Society of Intensive Care Medicine (ESICM), European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and Asociación Latinoamericana del Tórax (ALAT) Torres A, Niederman MS, Chastre J, et al. International ERS/ESICM/ESCMID/ALAT guidelines for the management of hospital-acquired pneumonia and ventilator-associated pneumonia. Eur Respir J 2017; 50: 1700582 [https://doi.org/10.1183/13993003.00582-2017].	• These guidelines were developed by a committee of 15 experts from the ERS, ESICM, ESCMID and ALAT and 2 methodologists. • The committee included specialists in respiratory medicine with expertise in the management of patients with lung infections, intensive care specialists, as well as microbiologists and methodologists with experience in evidence synthesis and guideline development. • Applying the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) methodology, the panel selected seven PICO (population–intervention–comparison–outcome) questions that generated a series of recommendations for HAP/VAP diagnosis, treatment and prevention. • The search was limited to human studies (systematic reviews, randomised clinical trials or observational studies) written in English. All searches were performed until	• The panel believes that performing routine bedside clinical assessments in patients receiving antibiotic treatment for VAP or HAP represents good practice. • Clinical evaluation usually involves measurement of temperature, tracheobronchial secretion volume, culture and purulence assessment of tracheobronchial secretions, evaluation for chest radiograph resolution, white blood cell count, arterial oxygen tension/inspiratory oxygen fraction (PaO2 /FIO2), and calculation of one or more scores such as CPIS, ODIN (Organ Dysfunction and Infection System), SOFA (Sequential Organ Failure Assessment), SAPS II (Simplified Acute Physiological Score II) and APACHE II.	Chest radiograph resolution	• We suggest obtaining distal quantitative samples (before any antibiotic treatment) to reduce antibiotic exposure in stable patients with suspected VAP and to improve the accuracy of the results. (Weak recommendation, low quality of evidence.) We recommend obtaining a lower respiratory tract sample (distal quantitative or proximal quantitative or qualitative culture) to focus and narrow the initial empiric antibiotic therapy. (Strong recommendation, low quality of evidence.) • The panel believes that tailoring antibiotic therapy to the susceptibility data of the aetiological pathogen once microbiological and clinical response data become available (day 3) represents good practice.	

	December 2014 and guideline panel members monitored the literature relevant to their assigned clinical question up to September 2016.				