Revista Argentina de Microbiología 58 (2026) 100715

REVISTA ARGENTINA DE MICROBIOLOGÍA

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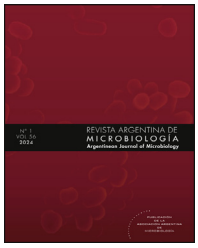

ORIGINAL ARTICLE

Recommendations for a microbiology Diagnostic Stewardship Program for antimicrobial resistance: Pre-analytical phase

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Received 15 July 2025; accepted 6 January 2026
Available online 31 March 2026

KEYWORDS
Diagnostic Stewardship;
Antimicrobial resistance;
Pre-analytical;
Antimicrobial stewardship;

Abstract Diagnostic Stewardship Programs (DSPs) in microbiology aim to ensure that the right diagnostic test is performed on the right patient at the right time, optimizing resource utilization. To maximize their effectiveness against antimicrobial resistance (AMR), DSPs must be integrated with Infection Prevention and Control (IPC) programs and Antimicrobial Stewardship Programs (ASPs). This article focuses on the pre-analytical phase of DSPs, specifically on test ordering, and additionally, it offers some recommendations for resource-limited settings. It presents a series of algorithms for ordering blood cultures, urine cultures, and respiratory specimens. A crucial concept in this phase is pretest probability, which guides rational test ordering, prevents overutilization and associated costs, and reduces laboratory workload.

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https://doi.org/10.1016/j.ram.2026.100715

ASP;
Recommendations for blood culture;
Urine culture;
Respiratory sample collection in pneumonia;
CAP;
HAP;
VAP

Regarding blood cultures, it is essential to standardize ordering criteria, prioritizing high-risk populations. Routine use is discouraged in cases of low pretest probability or when results do not alter clinical management. Blood volume and the number of bottles are critical for optimal yield. For urine cultures, it is fundamental to order them only when characteristic urinary symptoms are present, avoiding requests for asymptomatic bacteriuria or nonspecific symptoms. Finally, for respiratory specimens, the choice of diagnostic method should consider the patient's condition and available resources. Molecular techniques enhance pathogen detection, but must be integrated within an ASP for proper interpretation and rational antimicrobial use.

PALABRAS CLAVE
Optimización del diagnóstico;
Resistencia a los antimicrobianos;
Preanalítica;
Uso adecuado de antimicrobianos;
PROA;
Recomendaciones para hemocultivo;
Urocultivo;
Toma de muestra respiratoria en neumonía;
NAC;
NIH;
NAVM

Recomendaciones para un programa de optimización de diagnóstico en microbiología para la resistencia a los antimicrobianos. Fase preanalítica

Resumen Los programas de optimización de diagnóstico (PROD) en microbiología tienen como objetivo asegurar el diagnóstico adecuado en el paciente correcto y en el momento oportuno, optimizando el uso de los recursos. Los PROD deben integrarse con los programas de control de infecciones (PCI) y los programas de uso adecuado de antimicrobianos (PROA) para maximizar su efectividad contra la resistencia a los antimicrobianos (RAM). Este artículo se centra en la fase preanalítica de los PROD, abordando la solicitud, la recolección y el transporte de muestras mediante algoritmos específicos para hemocultivos, urocultivos y muestras respiratorias, incluyendo algunas recomendaciones para entornos con recursos limitados. En esta fase, la probabilidad pretest es fundamental para una solicitud racional de pruebas, evitando el sobreuso y sus costos asociados, así como la sobrecarga del laboratorio. En cuanto a los hemocultivos, es esencial estandarizar los criterios de solicitud, priorizando poblaciones de alto riesgo y desaconsejándose su uso en casos de baja probabilidad pretest o cuando el resultado no modifica el manejo clínico. El volumen de sangre y la cantidad de frascos son críticos para el rendimiento diagnóstico. Para los urocultivos, es fundamental solicitarlos solo ante síntomas urinarios característicos, evitando su solicitud en la bacteriuria asintomática o con síntomas inespecíficos. Finalmente, en cuanto a las muestras respiratorias, la elección del método diagnóstico debe considerar la condición del paciente y los recursos disponibles. Las técnicas moleculares mejoran la detección de patógenos, pero deben integrarse en un PROA para una interpretación adecuada y un uso racional de los antimicrobianos.

Introduction

Diagnostic Stewardship Programs (DSPs) in microbiology are initiatives designed to optimize the use of microbiological diagnostic tests to improve patient care and the management of infectious diseases. The goal of DSPs is to ensure the application of the right diagnostic method, in the right patient, and at the right time. These initiatives help optimize the use of diagnostic techniques and healthcare resources, reduce errors, and enhance the quality of patient care[20]. In the field of microbiology, DSPs are crucial for optimizing diagnosis, which in turn promotes a more efficient use of antimicrobials and helps mitigate antimicrobial resistance (AMR)[36]. Given the World Health Organization's declaration of AMR as a major global health threat, it is imperative to develop DSPs in conjunction with Infection Control Programs (ICP) and Antimicrobial Stewardship Programs (ASP), thereby maximizing their effectiveness. However, to achieve full effectiveness, these programs must function in an integrated manner. In the specific context of DSPs, active and coordinated collaboration with ASPs is particularly relevant and crucial for achieving common goals regarding AMR.

DSPs are fundamental for guiding the appropriate use of diagnostic tests, managing results, and directing antimicrobial prescribing. Furthermore, they provide essential information for ICPs and ASPs, such as local epidemiological data, which are vital for designing empirical treatments and implementing effective preventive interventions[42].

DSPs are structured into three phases: pre-analytical, analytical, and post-analytical. This article will focus exclusively on the pre-analytical phase of DSPs in microbiology, specifically for blood cultures, urine cultures, and respiratory samples. The pre-analytical phase spans from the request for microbiological studies to the collection and transport of samples. Its primary objective is to optimize the utilization of diagnostic tests, the collection of samples

to ensure accurate results, and the management of material and human resources[12].

A fundamental concept at this stage is pre-test probability, defined as the likelihood that a patient has a disease before a diagnostic test is performed. Considering that pre-test probability is crucial for the optimal use of diagnostic studies, ensuring the correct test is requested for the right patient and promoting the rational use of antimicrobials. Omitting this concept can lead to an overuse of diagnostic tests, which in turn results in an increased workload for laboratory personnel and inappropriate use of material resources (e.g., reagents, culture media), raising costs and exposing patients to unnecessary procedures[12].

A key strategy of DSPs is the design of diagnostic algorithms. These algorithms involve the implementation of predefined criteria, based on scientific evidence that determine the appropriate timing for performing specific tests. This guide focuses on addressing this stage, specifically on the design of these algorithms for diagnostic decision-making.

While the pre-analytical phase also includes fundamental aspects such as sample collection, transport, and storage, we recommend for an in-depth understanding of these topics to consult the recent *Guide to Utilization of the Microbiology Laboratory for Diagnosis of Infectious Diseases: 2024 Update* from the Infectious Diseases Society of America (IDSA) and the American Society for Microbiology (ASM), Clinical Infectious Diseases, 2024[35]. It is widely recognized that inadequate practices in collecting samples for cultures compromise their quality, hinder diagnosis, and frequently lead to increased unnecessary antimicrobial use. For this reason, these practices must be considered comprehensively within hospital DSPs[35].

This document proposes a guide for the implementation of an AMR-focused DSP in microbiology, aimed at an interdisciplinary team including microbiologists, infectious disease specialists, pharmacists, infection control specialists, physicians, nurses, physical therapists, and respiratory therapists. It is specifically oriented toward the diagnosis in adult patients treated in emergency departments and inpatient units. As mentioned, only recommendations related to the pre-analytical phase of blood cultures, respiratory samples, and urine cultures will be addressed, due to their significant impact on AMR managemen[12].

Recommendations for reading this document

To facilitate comprehension, each section of this document includes a detailed algorithm for ordering blood cultures, urine cultures, and respiratory samples. Immediately following each algorithm, a description of its contents is provided, organized into brief paragraphs. For example, within the blood culture algorithm, sections related to central line-associated infections will be numbered (e.g., 1), and this numbering directly correlates with the corresponding paragraph (paragraph 1) that describes that point in detail.

1. Recommendations for blood culture ordering

Blood cultures are a fundamental tool for identifying bacteremia, which is the presence of bacteria in the bloodstream. However, their indication in clinical practice can be inconsistent, leading to both underuse and overuse. Overuse involves the unnecessary collection of blood cultures, whose results do not alter the patient's therapeutic management, either at initial collection or in follow-up cultures. This translates into an inefficient use of resources and laboratory time. On the other hand, underuse, or the omission of appropriate blood culture requests, decreases the probability of identifying the causative pathogen, compromising patient outcomes and limiting antimicrobial de-escalation[10]. Given the morbidity and mortality associated with bacteremia, it is crucial to standardize blood culture ordering criteria in high-risk populations.

Furthermore, the contamination of samples during collection, resulting in false positives or ''pseudobacteremias,'' is a frequent concern. This situation can lead to misdiagnosis, prolonged hospitalization, unnecessary diagnostic tests, inappropriate antibiotic use, and increased costs[15]. In this regard, it is essential for each institution to evaluate and maintain its blood culture contamination rate at least below the 3% standard[10].

To optimize the diagnostic yield of blood cultures, two priority aspects are crucial: blood volume and the number of bottles requested. The volume of blood drawn is the most important variable for organism recovery[35]. At least two sets of blood cultures should be collected, requiring two venipunctures. Each set should include two to three blood culture bottles, containing 10 ml of sample each, ensuring the inclusion of at least one aerobic and one anaerobic bottle[35]. The aerobic blood culture bottle should be drawn first; drawing the aerobic bottle first minimizes the risk of introducing air into the anaerobic bottle, which could compromise the recovery of obligate anaerobes.

In situations of limited resources, at least three blood culture bottles with two venipunctures are advised (two bottles from one venipuncture and one bottle from the subsequent venipuncture), extracting 10 ml of blood per bottle. In this scenario, priority should be given to filling two aerobic bottles and one anaerobic to maximize diagnostic effectiveness within these constraints. For the pediatric population, the volume of blood to be cultured must be appropriate for the child's age and weight. The IDSA and ASM guidelines mentioned above should be consulted for specific recommendations in this population[35].

An algorithm proposing indications for blood culture ordering is shared below (Fig. 1).

1. Primary bloodstream infection (BSI) associated with a central venous catheter (CVC)

The diagnosis of primary bloodstream infection (BSI) associated with a central venous catheter (CVC) is based on recovering positive blood cultures, demonstrating that the catheter is the source of the infection, and excluding other possible primary sources of infection. Two peripheral venipuncture blood cultures (preferably before CVC removal) and one blood culture through the catheter or port (retro-culture) should be collected and processed in a continuous-monitoring blood culture system[32,35].

Routine culture of intravenous catheter tips upon removal lacks diagnostic value and should not be performed. Numerous studies have demonstrated its low

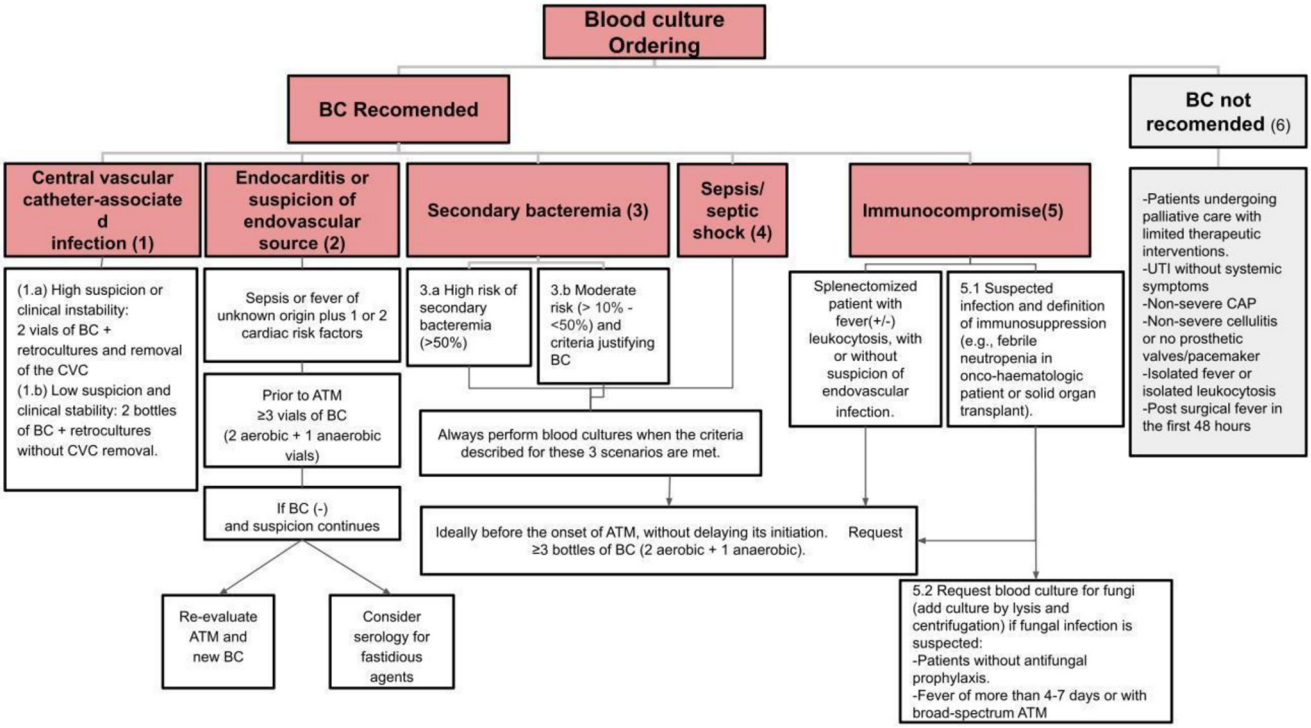

Figure 1 Indications for blood culture ordering. CVC: central venous catheter; BC: blood cultures; ATM: antimicrobials.

positive predictive value, minimal contribution to modifying the treatment of CVC-associated bacteremia, and results that are often delayed compared to those obtained from blood cultures[35,47]. Although they can occasionally suggest the origin of bacteremia, this diagnosis, as mentioned, is usually established by exclusion. Uncertainty about whether the CVC is the source or if it was contaminated by bacteremia from another source, further reduces its clinical utility. The most recent IDSA and ASM guidelines discourage their use[35]. While they might be useful in patients with a high pretest probability for CVC-associated infection, evidence shows that most CVC tip cultures do not alter clinical management[35,47]. Therefore, this practice is not included in the diagnostic optimization algorithms of this document. However, in institutions lacking automated blood culture systems, where the differential time to positivity between peripheral blood cultures and retrocultures cannot be applied, maintaining the practice of catheter tip culture and blood cultures as a diagnostic tool to evaluate the presence of catheter-related bacteremia is recommended[32].

Furthermore, it is important to consider that the probability of a catheter being the source of an infection is low when it has remained *in situ* for less than 48 h. Consequently, catheter-associated infection should not be suspected in these cases, unless the device was inserted in an emergency setting or under conditions that may have compromised adherence to aseptic technique standards[33].

1.a. Mortality in patients with sepsis or septic shock is lower when adequate source control is achieved, either through abscess drainage or catheter removal in potentially infected patients[27].

1.b. Immediate CVC removal may not be necessary in all cases. The decision should consider vascular accessibility, risk of complications from a new procedure, and the possibility that the CVC is not the source of the infection. To evaluate CVCs without removing them, peripheral blood cultures and retrocultures from each catheter lumen are recommended, inoculated with the same blood volume, at the same time and processed in a continuous monitoring system[27,35]. The frequent lack of simultaneous collection poses a considerable challenge when interpreting the differential time to positivity between catheter and peripheral blood cultures.

2. Infectious endocarditis

Infectious endocarditis (IE) remains a diagnostic challenge due to its variable clinical presentation, which can be acute or chronic. IE is suspected in the presence of fever and positive blood cultures without an alternative focus of infection, especially in patients with risk factors[9]. These risk factors can be cardiac (previous IE, prosthetic valves, congenital or rheumatic heart disease, degenerative valvular disease, ventricular assist devices, or cardiac electronic devices) or non-cardiac (central venous catheters, intravenous drug use, immunosuppression, recent dental or surgical procedures, recent hospitalization, hemodialysis)[9].

Although conventional blood culture methods are sufficient for most etiological agents of IE, certain less common etiologies require different diagnostic approaches[9]. These rare agents should be particularly suspected in culture-negative infectious endocarditis. *Bartonella* spp., *Coxiella burnetii*, and *Tropheryma whipplei* are often diagnosed using conventional serological tests or molecular amplification methods[35]. In Argentina, for the investigation of these specific etiologies in suspected cases, serum, whole blood,

and valvular vegetation samples can be sent to the National Reference Laboratory, Instituto Malbrán.

3. Secondary bacteremia

According to Fabre et al.[14], the utility of obtaining BCs (blood cultures) blood cultures (BCs) in this scenario should be evaluated, considering the following:

- The probability of bacteremia in different infectious conditions.
- The additional microbiological information gained compared to culturing the primary focus.
- The impact of the results on antimicrobial (ATM) decision-making.
- The impact of bacteremia on patient prognosis.

Taking these parameters into account, and based on the study by Fabre et al.[14], cases can be classified as:

3.a. High probability of bacteremia (>50%)

This category includes meningitis, endovascular infections, ventriculoatrial shunt infections, native vertebral osteomyelitis, epidural abscess, and non-traumatic native septic arthritis. In some of these, the yield of BCs is even higher than culturing the primary focus of infection (e.g., epidural abscess). Due to this characteristic, BCs are cost-beneficial and are recommended in all such cases.

3.b. Moderate probability of bacteremia (>10%–<50%)

This category includes cholangitis, pyelonephritis, cellulitis, and severe pneumonia (Pneumonia Severity Index [PSI] score IV or V, or admission to critical care, or ventilator-associated). In these scenarios, the yield from culturing the primary focus is higher than that of BCs. In this second case, even acknowledging a lower yield, obtaining BCs is recommended in the following situations:

- When the primary site of infection is not accessible, or when it is necessary to initiate antibiotic treatment before samples from the infectious focus can be obtained. For example, in acute cholangitis where a delay in performing an endoscopic retrograde cholangiopancreatography (ERCP) with bile sample collection for culture is anticipated.
- When the patient is at risk of endovascular infection (e.g., patients with endovascular prosthetic devices and bacteremia caused by *S. aureus*).
- When the presence of bacteremia could worsen the clinical outcome of the infection (e.g., patients with chronic renal failure, diabetes, or immunocompromise).
- When the BC results could modify ATM treatment.

4. Sepsis

Early blood culture collection is recommended whenever sepsis and septic shock are suspected, as identifying an etiological diagnosis is crucial[41]. Blood cultures should ideally be collected before initiating antimicrobial therapy, without delaying its administration.

The dilemma lies in the definition of sepsis and septic shock. Low specificity in the definitions of sepsis and septic shock can lead to the overuse of blood cultures and antimicrobials, as well as an inadequate clinical diagnosis. Conversely, low sensitivity could result in inappropriate patient management and increased mortality. Properly defining both conditions is necessary to optimize the management of these patients[11].

Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection. Unlike previous definitions that linked sepsis with a qSOFA change $\geq$2, recent ''Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2021'' discourage the exclusive use of qSOFA due to its low sensitivity. Instead, combining it with other tools such as SIRS, NEWS, or MEWS[44] is recommended.

Septic shock is a condition of sepsis with circulatory and metabolic abnormalities that is severe enough to increase the risk of mortality. That is, a condition of sepsis accompanied by hypotension (MAP < 65 mmHg) requiring vasopressors despite adequate fluid resuscitation, along with a lactate level >2 mmol/l[44].

5. Immunocompromised patients

Immunocompromised patients face an increased risk of developing sepsis and bacteremia[25,39]. In this population, accurate and early diagnosis is crucial for initiating appropriate antimicrobial therapy. Implementing prediction models improves the precision of an early diagnosis. Pawlowicz et al. demonstrated a reduction in blood culture requests in the emergency department through a clinical decision tool designed to standardize this practice[39]. Among the criteria included in this tool are immunocompromise and hemodynamic instability.

5.1 Definition of severe immunosuppression

Severe immunosuppression is defined by the presence of the following criteria: active leukemia or lymphoma, disseminated malignant disease, aplastic anemia, graft-versus-host disease (GVHD), congenital immunodeficiencies (e.g., common variable immunodeficiency), treatment with checkpoint inhibitors or recent radiation therapy, solid organ transplant with immunosuppressive treatment, transplant-related immunosuppressive drugs: cyclosporine, tacrolimus, sirolimus, everolimus, azathioprine, mycophenolate mofetil, hematopoietic stem cell transplant (HSCT) recipients within two years or those still on immunosuppressive drugs, high-dose systemic corticosteroids (20 mg or more of prednisone daily or equivalent) for at least two weeks, alkylating agents (cyclophosphamide) or antimetabolite agents methotrexate (>0.4 mg/kg/week); azathioprine ($\geq$3 mg/kg/day) or 6-mercaptopurine ($\geq$1.5 mg/kg/day), chemotherapeutic agents for cancer, tumor necrosis factor alpha blockers (etanercept, adalimumab, certolizumab, golimumab, infliximab), biologics, lymphocyte-depleting agents like thymoglobulin or alemtuzumab, B-cell depleting agents like rituximab, HIV patients with a CD4 count <200 cells/mm, AIDS diagnosis, or symptomatic HIV[25]. Neutropenia is typically defined as an absolute neutrophil count (ANC)

<1500 or 1000 cells/μL. Severe neutropenia is considered when the ANC is <500 cells/μl or is expected to decrease to <500 cells/μl within the next 48 hs. Finally, profound neutropenia is defined as an ANC <100 cells[18,24].

Initial blood cultures at the start of empiric antibiotic therapy for febrile neutropenia (FN) are essential. However, the clinical relevance of repeat blood cultures in cases of persistent or recurrent FN after the initiation of empiric antibiotics is not well-established. The IDSA guidelines do not recommend routine repeat blood cultures for persistent fever after four days of FN, unless there is a change in the patient's clinical status[18,24]. Repeated blood cultures are recommended if there is suspicion of an endovascular or epidural focus, a retained device, neutropenic enterocolitis, risk factors for multidrug-resistant organisms, hemodynamic instability, events suggestive of a new infection site, or previous isolation of organisms such as *Staphylococcus aureus* or *Candida* spp.[18,24]. Persistent fever after defervescence with antibiotics should be interpreted as a possible new infectious event. The yield of repeat blood cultures in patients with persistent febrile neutropenia can be improved by using risk models that predict bacteremia. Symptoms such as chills, fever ≥38 °C, and a history of recent bacteremia episodes are key indicators.

5.2 Blood culture requests for fungal infection

Blood cultures to document fungal infection in severely immunocompromised patients should be performed in those who present with persistent fever for more than 4–7 days, despite being on a broad-spectrum antibiotic regimen. This practice is especially relevant in patients not receiving antifungal prophylaxis.

6. Situations where blood culture collection is not recommended

Evidence suggests a lower pre-test probability of positivity or a low diagnostic yield for blood cultures in certain infectious diseases. Additionally, in some cases, a positive blood culture does not lead to changes in patient management[50]. In these situations, blood cultures are not recommended.

Blood culture collection is discouraged in situations where the probability of bacteremia is low (<10%). This includes, but is not limited to, fever within the first 48 h post-surgery, non-severe pneumonia, and cystitis/prostatitis, for which there is sufficient data to support this recommendation[14,28,31,50]. Furthermore, bacteremia is uncommon in patients with non-severe purulent or non-purulent cellulitis. Another situation where this practice should not be considered, as it does not lead to changes in patient management, is in the case of patients under palliative care with limited therapeutic interventions[29].

7. Other considerations regarding blood culture collection

a. Number of venipunctures, bottles, and blood volume

Tradtionally, blood culture collection recommends two venipunctures. The purpose of this practice is to distinguish the presence of a contaminated blood culture by taking samples from two different sites. However, recent studies have explored the collection of a larger volume of blood (40 ml) via a single venipuncture, distributed into four bottles (10 ml/bottle), which improves patient comfort[30]. This strategy, however, carries a risk of contaminating at least two bottles with skin flora if the aseptic technique is deficient, potentially leading to an erroneous diagnosis of bacteremia. Therefore, its implementation demands strict rigor in aseptic protocols.

Some studies have shown that the contaminated blood culture rate is similar between single and multiple venipunctures, although the diagnostic yield in terms of positive blood cultures is superior using the single-puncture technique[43]. This approach could be acceptable in institutions with a low rate of contaminated blood cultures (while a rate below 3% is acceptable, the goal should be 1%)[32]. Its diagnostic efficacy without increased contamination has been observed in critical care units[48].

In summary, while current promising results suggest a possible re-evaluation of the blood culture collection approach, further research is crucial to validate its implementation in diverse clinical settings prior to adopting it as standard practice. Currently, two venipunctures are still recommended. Nevertheless, if an alternative strategy is chosen, it is necessary to reinforce the blood culture collection technique, maintain a low contamination rate, notify the laboratory, and ensure this detail is clearly specified on the sample label.

b. Which situations require a follow-up blood culture?

- For bacteremia follow-up and therapeutic efficacy evaluation, repeat blood cultures are recommended between 2 and 4 days for *S. aureus*, *Staphylococcus lugdunensis*, and *Candida* spp. to document clearance. It is crucial to consider the ''skip phenomenon,'' where initial blood cultures may yield false negatives while subsequent ones are positive. Some experts suggest obtaining at least four blood cultures during the follow-up of *S. aureus* bacteremia[5,48].
- Endocarditis or other endovascular infections[5,48].
- Deep suppurative infection or foci not resolved by immediate surgical intervention (e.g., multiple abscesses)[9].
- Limited therapeutic options: In cases where no evidence-based therapeutic options exist, or when off-label or compassionate use treatments are being utilized.
- Persistence of fever or septic equivalents beyond 72 h of effective treatment, with adequate administration route and dose, and controlled source[5,48].
- Inability to use the best therapeutic option, due to allergy, severe pharmacodermia, or severe systemic adverse effects.
- Unidentified infection source or no clinical improvement in patients without a clear source of infection, or not showing clinical or laboratory improvement.

c. Blood culture sample collection checklist[35]

- Hand hygiene with soap and water or use of alcohol-based hand rub.

- Preparation of blood culture bottles: Disinfection of the rubber cap using a gauze soaked in 70% alcohol; avoid use of iodine-based products.
- Preparation of sterile gauzes and syringes for collection. Avoid contaminating the syringe during package opening.
- Hand hygiene with soap and water or use of alcohol-based hand rub.
- Use of sterile gloves or examination gloves.
- Use of a disposable glove or examination glove as a tourniquet.
- Selection of the puncture site.
- Skin disinfection with a sterile gauze soaked in alcohol-based chlorhexidine. Apply the antiseptic in a circular motion from the inside out, only once, and allow it to dry in accordance with the manufacturer's recommended time.
- Perform the blood draw without re-palpating the area. In case of difficult extraction, use sterile gloves to avoid contaminating the puncture site.
- Inject blood into the bottle held in a vertical position, allowing 10 ml of blood for adult patients. Do not invert the bottle for filling.
- At least 3 bottles should be filled: 2 aerobic and 1 anaerobic. The aerobic blood culture bottle should be drawn first.
- No waiting is necessary between punctures.
- No needle change is required between the extraction and injection of blood into the bottle.
- Do not recap the needle. Dispose of the needle and syringe in the nearest rigid sharps container.
- Label the bottles with the patient's information and send them immediately to the laboratory.

Recommendations for urine culture ordering

DSPs designed to optimize the indications for urine culture collection are an essential tool for preventing inappropriate antimicrobial use and related resistance[4]. This section will discuss potential strategies to optimize urine culture indications, including a proposed algorithm (Fig. 2). Several studies have shown that implementing algorithms to guide urine culture requests is effective in avoiding unnecessary tests and reducing the prescription of inappropriate antimicrobials[2,26,46]. Several studies have demonstrated that collaboration with the nursing team to support the implementation of these algorithms, with a prior educational phase, can successfully reduce unnecessary urine culture orders[13,46].

1. Patient with suspected urinary tract infection (UTI) and without a urinary catheter

The decision to collect samples is of vital importance, and they should only be requested when the patient without a urinary catheter exhibits characteristic urinary signs and symptoms.

1.1. The classic symptoms of UTI are dysuria, pollakiuria, bladder tenesmus, urinary urgency, hypogastric pain, and eventually flank pain and fever[35]. Atypical symptoms may include non-specific abdominal pain, urinary retention, fever, chills, hematuria, clinical instability (tachycardia, hypotension, sepsis or septic shock), provided that other causes that could explain these symptoms have been ruled out[4]. Alterations in mental status or changes in urine odor or color are not considered, *per se*, symptoms of UTI[4]. The inclusion of urine cultures should be avoided in[4]:

- Standard order sets (e.g., routine health exams, emergency department evaluations or hospital admissions, presurgical exams in non-urological patients, evaluations for altered mental status or falls in chronic care).
- Cases with non-specific symptoms (e.g., asthenia or decreased appetite) without evidence of systemic infection or UTI, or in the presence of dysglycemia.
- Response to changes in urine characteristics or pyuria in asymptomatic patients.
- Documentation of cure (follow-up urine culture) or after urinary catheter change.

Various studies have demonstrated the effectiveness of implementing best practice alerts in clinical information systems. These alerts aim to discourage the request for urine cultures in the absence of clinical signs or symptoms suggesting a UTI[4]. Automatic cancellation of repeat urine cultures within 5 days of a positive culture (during the same hospital admission and 7 days for residents of long-term care facilities) can also be an effective strategy[4].

1.2. The clinical diagnosis of UTI can be challenging. It is important to remember that some special populations, such as the elderly, immunocompromised patients, or pregnant women, may be oligosymptomatic. It is worth mentioning that multiple medical conditions can present with symptoms similar to those of a UTI and even show an increase in leukocytes in the urine[4].

The differential diagnosis for UTI varies by population. For women of all ages, conditions to consider include vaginitis, genital herpes, irritative cystitis (due to physical or chemical irritants), and lichen sclerosus. In postmenopausal women, vaginal atrophy and superior pelvic floor prolapse are also relevant differential diagnoses. For men, epididymitis, urethral trauma, and prostate hyperplasia should be considered. Finally, for both sexes, the differential diagnoses include vesical/renal lithiasis, sexually transmitted diseases, contact dermatitis, low back pain, diabetes, diuretic use, and bladder cancer[4].

1.3 In older adults, a population frequently subject to inappropriate antimicrobial use for suspected UTIs, it is crucial to emphasize that altered mental status alone, without other suggestive UTI signs or symptoms, does not warrant urine sampling. Similarly, treating asymptomatic bacteriuria in functionally or cognitively impaired older adults, with or without a history of falls, is not recommended due to a lack of demonstrated clinical benefit, and also the risk of fostering antimicrobial resistance and treatment-related adverse events. For this demographic, utilizing scores such as the BLADDER score (Blood in urine: 1 point, Loss of urinary control: 1 point, Abdominal pain: 1 point, Dysuria: 2 points, Elevation of temperature (>38 °C): 1 point, Repeated urination: 1 point) might be beneficial for guiding urine culture decisions in patients without catheters. A score of 0–1 suggests no urine culture is needed, while a score of 2–7 indicates that a urine culture should be sent, with treatment

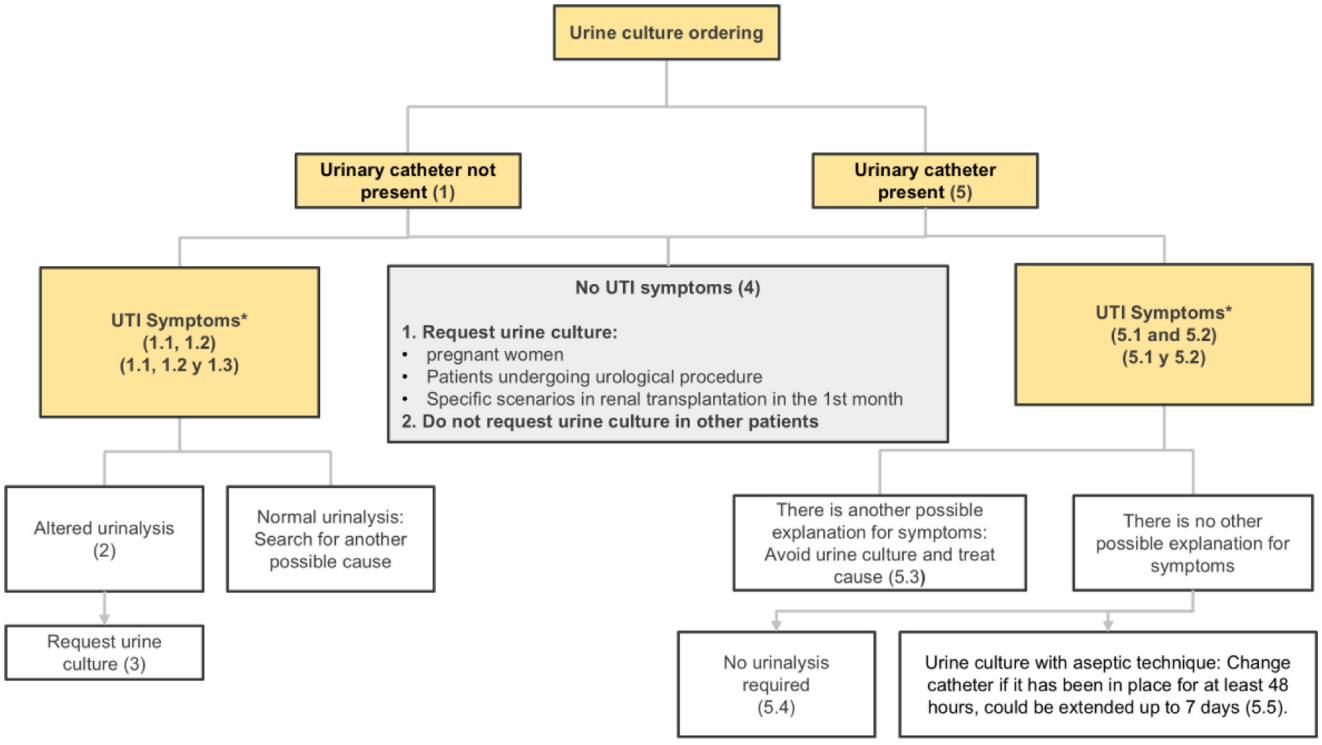

Figure 2 Indications for urine culture ordering. *UTI typical symptoms: dysuria, pollakiuria, bladder tenesmus, urinary urgency, hypogastric pain, and eventually low back pain and fever. Atypical symptoms: nonspecific abdominal pain, urinary retention, chills, hematuria, clinical instability (tachycardia, arterial hypotension, sweating, or septic shock).

initiated only if a UTI is suspected, followed by reevaluation upon culture results. Additionally, routine urinalysis is not recommended in this study due to its low specificity for UTI diagnosis in this population[26].

2. Urine analysis

To optimize the request for urine cultures and reduce unnecessary studies, we recommend replacing the isolated indication of a urine culture in patients with suspected UTI with a combined approach that includes a urine analysis (UA). Healthcare teams should establish institutional consensuses to process urine cultures only from samples that show alterations in the UA[7,8]. Studies have shown that pyuria is a good marker in terms of negative predictive value, that is, the presence of a UTI is considered unlikely when there is no significant leukocyturia[2]. The presence of more than 10 leukocytes per high-power field in the UA is commonly accepted as a cutoff point[2] (Table 1). Urine analysis and predictive values for identifying a positive urine culture[2,19].

3. Urine culture collection and transport

For a detailed description of urine culture collection techniques, refer to the mentioned guidelines from IDSA and ASM[35]. However, as a concise reminder, urine samples should be obtained using the ''midstream clean catch'' technique or via catheterization, ideally after at least 3 h of urinary retention, with the first morning urine being the optimal sample. Laboratories are advised to provide detailed instructions to patients to ensure proper sample collection. For patients that need assistance, urine culture collection should be performed by trained professionals using the aseptic technique. Samples obtained by cystoscopy or suprapubic aspirations must be clearly identified. Prostatic massage is not recommended in acute prostatitis due to its limited diagnostic value and the risk of bacteremia.

A minimum of 10 ml of urine should be collected in a sterile container. It must be transported immediately to the laboratory. Urine collected for culture should be refrigerated (2–8 °C) if processing is delayed for more than 30 min post-collection, remaining viable for up to 24 h before processing.

4. Asymptomatic bacteriuria (ASB)

4.1 Definition and screening recommendations

ASB is defined as the presence of bacteria in urine at a count of $\geq 10^5$ colony-forming units per milliliter (CFU/ml) in two consecutive urine samples from women, or one sample from men, in the absence of signs and symptoms of a UTI, regardless of the UA[37].

Currently, screening and subsequent treatment of ASB are advised only in the following patient groups[4,35]:

- Pregnant women
- Patients scheduled for urological procedures that involve mucosal bleeding
- In specific situations for renal transplant recipients in the first month.

Table 1 Urine analysis and predictive values for identifying a positive urine culture[37,41]

	Positive predictive value	Negative predictive value	Comments
Pyuria	For a positive urine culture: 32–37% according to leukocyte count 5–20 per field.	To rule out UTI: 89% to 95% depending on leukocyte count of 20-5 per high power field.	Limited utility in: Postmenopausal women Neutropenic patients Patients with long-term indwelling urinary catheters
Nitrite reductase reagent strips	≅90% Some pathogens such as *S. saprophyticus*, *S. aureus*, *Enterococcus*, *Pseudomonas*, *Acinetobacter*, and *Candida* do not convert nitrates to nitrites.	≅86%	Limited utility in postmenopausal women. Combination of pyuria and nitrites: better results than pyuria alone for ruling out UTI, especially in men and in patients >65 years.

Most guidelines recommend performing a urine culture during one of the initial visits at the beginning of pregnancy. There is insufficient evidence for or against repeating urine cultures during pregnancy in women with an initial negative urine culture or after treatment for an initial episode of ASB[37].

In renal transplant recipients, not to perform urine cultures or treat ASB after the first month post-transplant is recommended. However, there is insufficient evidence to support a recommendation for or against the detection or treatment of ASB within the first month after renal transplantation[37]. Typically, they are only performed in specific situations during the first month, and not routinely, such as when a biopsy is needed or for changes in renal function not explainable by other causes. Furthermore, screening for asymptomatic bacteriuria is not recommended in solid organ transplant recipients of other organs.

4.2 Prevalence and avoidance of unnecessary screening

Except for the three situations indicated above, ordering urine cultures in patients without symptoms consistent with a UTI should be avoided. The prevalence of ASB varies significantly depending on the studied population, from highest to lowest[6]:

- Individuals with prolonged indwelling urinary catheter use: 100%
- Individuals with spinal cord injury and intermittent catheter use: 23–69%
- Individuals with spinal cord injury and sphincterotomy/condom catheter: 57%
- Women aged 70 years or older in a chronic care facility: 25–50%
- Men aged 70 years or older in a chronic care facility: 15–50%
- Kidney transplant recipients
  - First month post-transplant: 23–24%
  - 1 month to 1 year post-transplant: 10–17%
  - 1 year post-transplant: 2–9%
- Men aged 70 years or older in the community: 3.6–19%
- Women aged 70 years or older in the community: 10.8–16%
- Women with diabetes: 10.8–16%
- Men with diabetes: 0.7–11%
- Pregnant women: 1.5–9.5%
- Women aged 50–70 years: 2.8–8.6%
- Premenopausal women: 1–5%
- Young men: Low, close to 0%

One population in which treatment of asymptomatic bacteriuria is frequently observed and should be avoided is patients with spinal cord injury. Screening for asymptomatic bacteriuria in this population is not recommended.

Treating asymptomatic bacteriuria, far from providing any clinical benefit to the patient, is associated with negative outcomes such as the occurrence of adverse effects, drug interactions, increased antimicrobial resistance, *Clostridioides difficile* infections, and increased costs[37].

5. Patients with urinary catheter or indwelling catheter and suspected urinary tract infection (CAUTI)

It is important to emphasize that systematic screening for asymptomatic bacteriuria is not indicated, nor is the treatment of positive urine cultures in the absence of clinical symptoms. This practice is fundamental to preserve available therapeutic options for these patients when they genuinely need them, thus avoiding the selection of multidrug-resistant organisms and unnecessary exposure to antimicrobial adverse effects.

5.1 Decision to perform urine culture: The decision to collect a urine sample must be based on symptoms, clinical conditions, and risk factors for severe infection (e.g., immunocompromised patients, ICU admission). CAUTI is a frequent cause of bacteremia[17,21].

5.2 In patients with a urinary catheter, local UTI symptoms are often absent, and the diagnosis is based on the presence of systemic signs and symptoms: fever, chills, hypotension, in the absence of another focus of infection. Non-specific signs and symptoms may include hypogastric pain, loin pain and acute hematuria[17,21].

5.3 Other causes of urinary symptoms may exist beyond UTIs. Therefore, it is crucial to perform a comprehensive evaluation of the patient, rule out other possible

foci of infection, other genitourinary infections, or other non-infectious causes that explain the patient's clinical presentation.

5.4 UA in catheterized patients may not be useful in the diagnosis of CAUTI due to the high probability of a result associated with an inflammatory process. In these cases, the presence of pyuria should not be interpreted as a sign of urinary infection or as an indication for antibiotic treatment[17,21].

5.5 The indwelling catheter for urine culture collection should be changed if it has been in place for at least 48 h or more, potentially extending up to a maximum of 7 days, depending on possibilities and patient characteristics. The risk of indwelling catheter colonization increases with the days of catheterization, reaching 100% after one month of permanence[17,21,43].

Recommendations for respiratory sample collection in patients with suspected pneumonia

Respiratory samples are vital for determining the cause of community-acquired (CAP), hospital-acquired (HAP), and ventilator-associated pneumonia (VAP), conditions linked to high morbidity and mortality. However, healthcare workers face challenges in interpreting microbiological results, particularly in distinguishing between true pathogens and harmless colonizers in the respiratory tract[40]. Optimizing the use of diagnostic tests is crucial to avoid unnecessary testing and/or delays in pathogen identification.

Historically, identifying causative agents in community-acquired pneumonia (CAP) was challenging due to the absence of rapid, accurate, and cost-effective diagnostic tools. However, molecular biology techniques have significantly advanced, enabling the swift and precise identification of various pathogens, including respiratory bacteria and viruses such as SARS-CoV-2 and influenza. These methods provide high sensitivity and specificity, delivering results much faster, which is crucial for effective disease management[19].

In VAP, non-specific or isolated symptoms such as hypotension, fever, or changes in secretion color heighten the risk of overdiagnosis and overuse of microbiological and molecular tests. While cultures are crucial for diagnosing both VAP and HAP, differentiating true pathogens from colonizers in hospitalized patients can be challenging. Therefore, respiratory samples should only be requested for patients who clearly meet clinical, imaging, and laboratory criteria for pneumonia. The selection of samples and diagnostic methods must consider the patient's clinical severity, available resources, staff expertise, and the ability to collect the sample promptly[40]. Microbiological diagnosis of pneumonia involves collecting various types of respiratory samples, including sputum, induced sputum, bronchoalveolar lavage (BAL), and tracheal aspirate. The choice of sample type depends on the patient's clinical situation and the suspected pathogen. The rational use of molecular tests and traditional microbiological techniques should aim to yield cost-effective results to guide antibiotic treatment, minimizing unnecessary antimicrobial exposure and improving clinical outcomes[12,23].

We propose two diagnostic algorithms to guide the request for microbiological studies in patients with clinical presentations consistent with CAP and HAP), respectively. Additionally, a third graphic outlines the specific laboratory tests indicated for respiratory samples from patients with HAP/VAP (Figs. 3–5).

1. CAP is an acute lower respiratory tract infection caused by a community-acquired organism. Diagnosis requires two or more of the following signs or symptoms: temperature >38 °C or ≤36 °C, cough, new or changed sputum production, dyspnea, tachypnea, pleuritic chest pain, in conjunction with consistent radiological findings[49]. Due to the low sensitivity of clinical signs and symptoms for CAP diagnosis, a chest X-ray is mandatory, even in resource-limited settings[49].
2. The decision regarding outpatient or inpatient management (general ward or ICU) is guided by clinical judgment and validated diagnostic scores, including the Pneumonia Severity Index (PSI) and CURB-65[15,16].
3. For most outpatient CAP cases, microbiological diagnosis (conventional culture or molecular methods) is not routinely necessary. This is primarily due to the high cost associated with such testing and its minimal impact on clinical or therapeutic management. However, optional testing may be considered for public health-relevant pathogens or those that could facilitate antibiotic de-escalation, such as Influenza virus or SARS-CoV-2[35].
4. In patients presenting with pleural effusion, it is advisable to perform physicochemical analysis of pleural fluid, cytology, direct examination, and culture for common pathogens, notwithstanding the often low microbiological yield from such examinations[35].
5. Blood cultures are positive in only 5–10% of CAP cases and rarely impact clinical management. For hemodynamically stable critical care patients, blood cultures are considered when other potential infection sources are suspected. However, in ICU patients with severe presentations – including hemodynamic instability, mechanical ventilation, or risk factors for *Pseudomonas* or MRSA – blood cultures are recommended[35,49].
6. The acquisition of high-quality respiratory samples is paramount for accurate microbiological diagnosis. These samples are characterized by a microscopic field exhibiting >25 polymorphonuclear leukocytes and <10 epithelial cells prior to culture. Samples demonstrating significant contamination with oropharyngeal microbiota or those not indicative of deep expectoration should be dismissed. Utilizing non-representative samples will inevitably lead to erroneous results, thereby compromising both diagnosis and subsequent treatment. This principle holds true for all analytical methods, encompassing both conventional microbiological studies (e.g., Gram stain and culture) and molecular tests[19,35].
7. Respiratory virus screening (Influenza, SARS-CoV-2, RSV) is recommended for hospitalized patients, particularly considering seasonality, using nasal or nasopharyngeal swabs. The choice of diagnostic method depends on methodological availability, ranging from antigen detection via immunofluorescence or immunochromatography to viral genome detection using molecular methods[47]. While molecular methods offer higher sensitivity

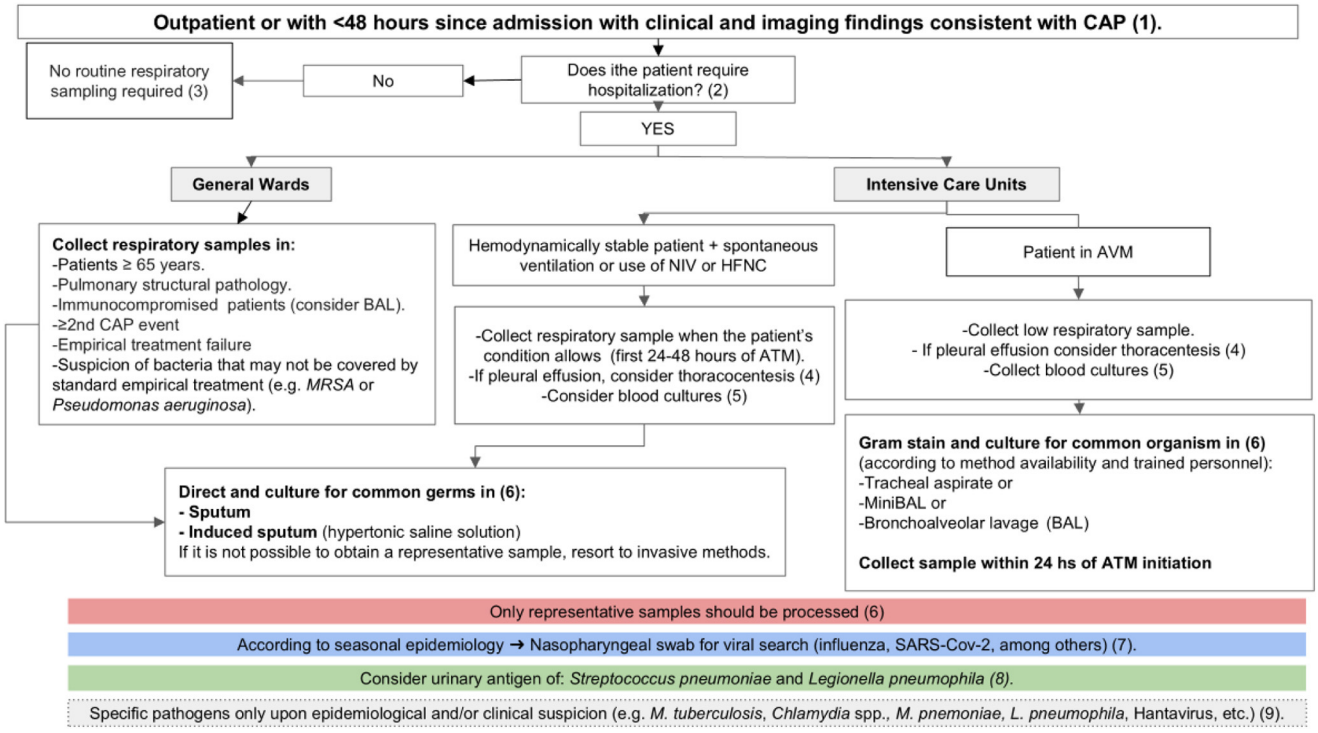

Figure 3 Diagnostic algorithm for community-acquired pneumonia (CAP). MRSA: methicillin resistant *Staphylococcus aureus*; HFNC: high-flow nasal cannula; LFNC: low-flow nasal cannula; MV: mechanical ventilation; CT: computed tomography; NIV: noninvasive ventilation; ATM: antimicrobials.

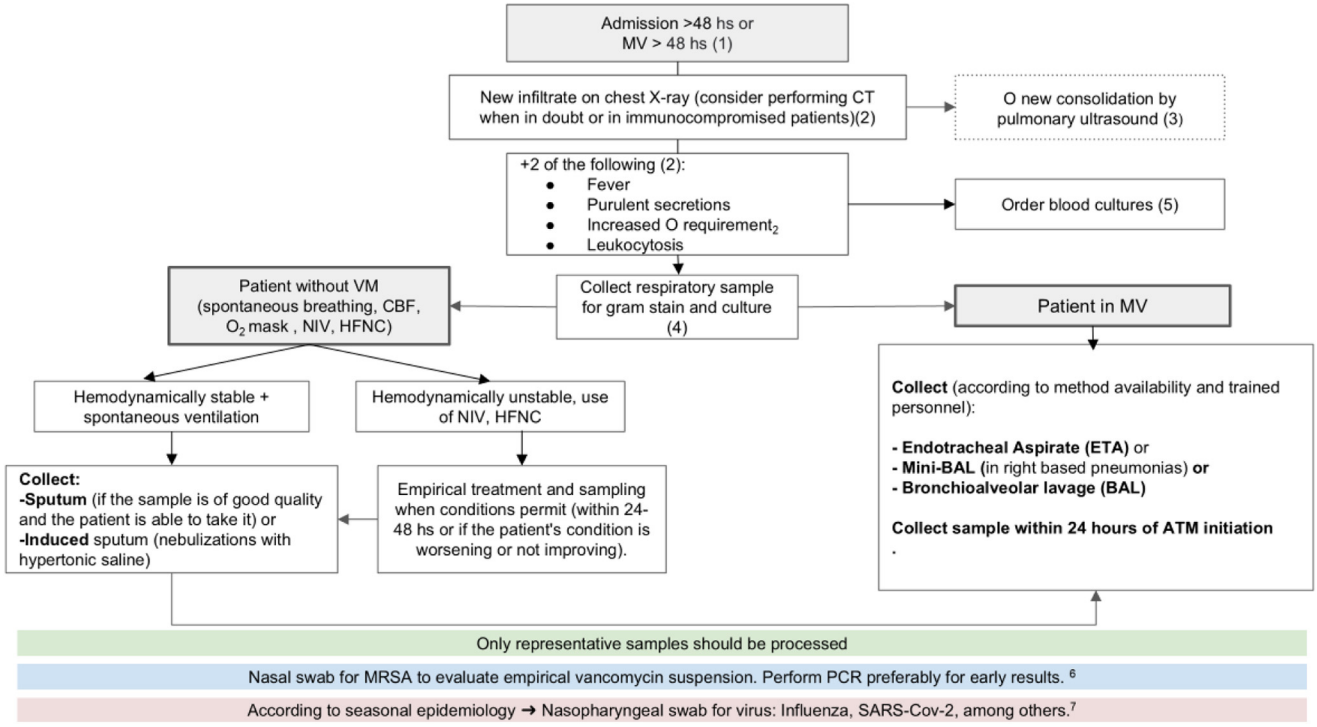

Figure 4 Diagnostic algorithm for hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP). HFNC: high-flow nasal cannula; LFNC: low-flow nasal cannula; MV: mechanical ventilation; CT: computed tomography; NIV: noninvasive ventilation; ATM: antimicrobials.

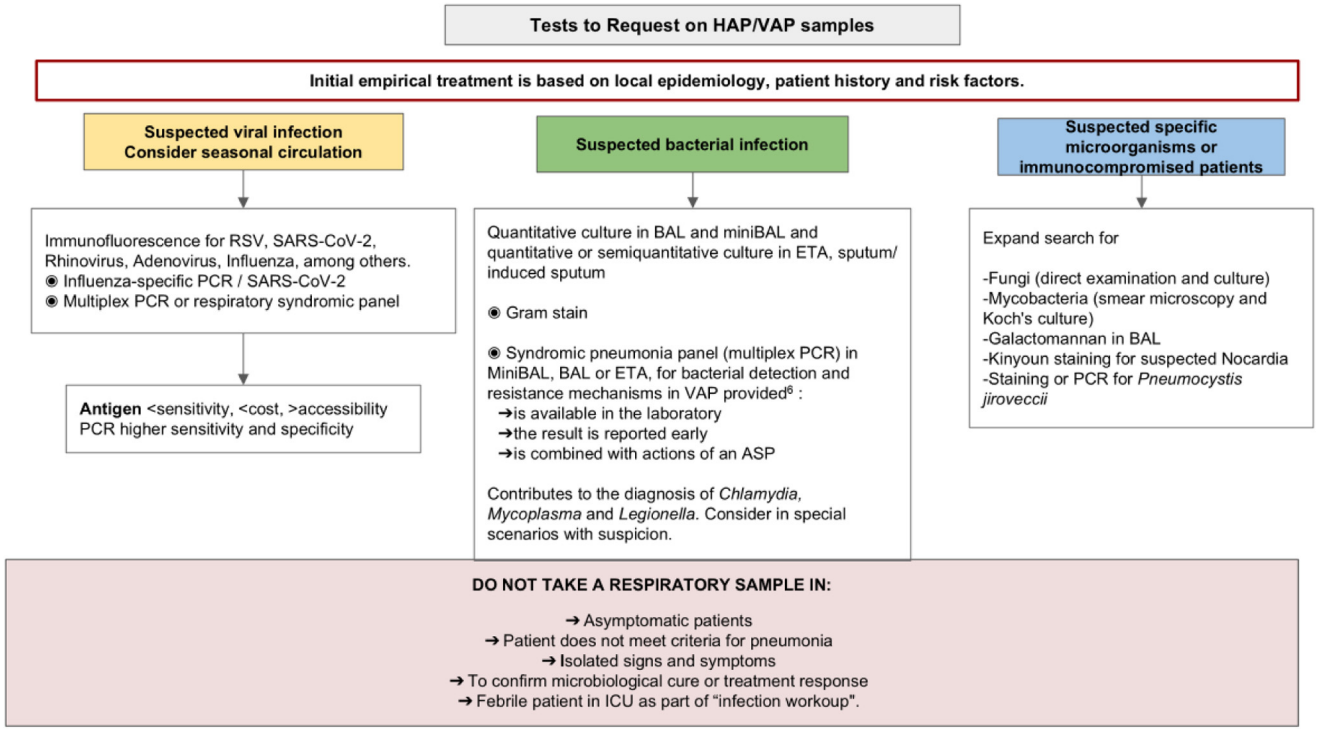

Figure 5 Laboratory tests to request for respiratory samples from patients with HAP/VAP. PCR: polymerase chain reaction; RSV: respiratory syncytial virus; BAL: bronchoalveolar lavage; ETA: tracheal aspirate; ICU: intensive care unit.

compared to rapid antigen detection, they may be less accessible and more costly.

Multiplex PCR methods and commercial syndromic panels, which detect a range of respiratory viruses and bacteria (e.g., *Chlamydia pneumoniae*, *Mycoplasma pneumoniae*), should be implemented within an ASP. When resources allow, viral panels are advised for critically ill patients in the ICU or those who are immunocompromised. For patients admitted to general wards, a more focused viral study (Influenza/SARS-CoV-2/RSV), preferably by PCR or antigen detection, is recommended. The timely detection of respiratory viruses can facilitate antibiotic discontinuation[15].

8. Consider urinary antigen detection for *Streptococcus pneumoniae* in severe pneumonia cases admitted to the ICU[15].

   For the detection of soluble urinary *Legionella pneumophila* antigen, it is important to note that the available method primarily detects serogroup I. Despite this specificity, serogroup I is implicated in 90% of *Legionella* infections. Therefore, its use is recommended in severe CAP, especially in patients with epidemiological risk factors, during outbreaks, or when there is no response to standard treatment for common pathogens[18,35].
9. Targeted pathogen investigation for organisms such as *Chlamydia spp.*, *Chlamydia psittaci*, *Mycoplasma pneumoniae*, *Bordetella spp.*, *Leptospira spp.*, Hantavirus, and *Pneumocystis jirovecii* should only be considered when guided by strong clinical suspicion and/or relevant epidemiological history[18,35].

Diagnostic algorithm for hospital-acquired pneumonia (HAP) and ventilator associated pneumonia (VAP) (Fig. 4):

1. HAP is defined as lung parenchymal infection developing more than 48 h after hospital admission. VAP occurs in patients receiving mechanical ventilation for over 48 h[7,45].
2. The diagnostic algorithm for HAP/VAP aims to differentiate VAP from other respiratory conditions in ventilated patients, facilitating rational antimicrobial use and timely treatment. Chest radiography is the most accessible initial assessment tool, though its sensitivity in ventilated patients is limited and often non-specific. Chest computed tomography (CT) is recommended for inconclusive findings and in immunocompromised individuals[7,38]. Worsening ventilatory parameters are also crucial and are recognized as diagnostic criteria by the U.S. Centers for Disease Control and Prevention (CDC)[3,38].
3. Lung ultrasound (LUS) provides a rapid, non-invasive assessment, eliminating the need for patient transfer and radiation exposure. While its efficacy is operator-dependent, LUS is gaining recognition for its value in VAP diagnosis, despite current limitations in evidence. Challenges may arise in obese patients or those with subcutaneous emphysema or chest wall edema. A systematic review and meta-analysis reported an 88% sensitivity and 89% specificity, positioning LUS as a safe, alternative diagnostic method when performed by trained personnel[3,38].

4. The etiology of HAP and VAP is predominantly bacterial and varies with institutional epidemiology. Given the non-specific nature of clinical diagnosis and the high likelihood of multidrug-resistant (MDR) organisms, especially in VAP, obtaining pre-treatment culture samples is recommended to complement diagnosis without delaying antibiotic initiation, particularly in unstable patients. While cultures are integral to HAP/VAP diagnosis, distinguishing true pathogens from contaminants or colonizers is often difficult, especially in critical care patients or those with comorbidities or tracheostomies[12].

   For non-ventilated HAP, sputum is the preferred sample if representative (defined as $\geq$25 polymorphonuclear leukocytes and $\leq$10 epithelial cells per direct microscopic field); induced sputum can facilitate collection. However, sputum has a low diagnostic yield (23–73% sensitivity). For VAP, non-invasive methods like endotracheal aspirate (ETA) with semi-quantitative or quantitative cultures ($\geq 10^6$ CFU/ml) demonstrate similar efficacy to invasive methods such as BAL or mini-BAL with quantitative cultures[1]. While ETA is simpler to obtain, invasive samples with quantitative cultures are more specific for distinguishing pathogen from contaminants, using lower cut-offs ($\geq 10^4$ UFC/ml in BAL and mini-BAL samples)[22]. Lower counts are considered potential contaminants or colonizers. Sample selection depends on hospital resources and staff training, prioritizing early collection before empirical antibiotic therapy.
5. Blood cultures can be a useful diagnostic tool in patients with hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP), though their diagnostic yield is limited, with positivity rates typically ranging from 10 to 20% in confirmed cases. Despite this low overall positivity, their utility is reinforced in severe clinical presentations, such as severe sepsis or septic shock, where the likelihood of concomitant bacteremia is higher[14,22]. Furthermore, similar to CAP, blood cultures are more valuable when there is suspicion of pneumonia concurrent with other potential sources of infection. Their use is also highlighted in patients for whom respiratory sample collection is contraindicated (e.g., those on non-invasive ventilation).
6. VAP caused by methicillin-resistant *S. aureus* (MRSA) is linked to poorer clinical outcomes, often necessitating broad-spectrum empirical antibiotics despite its low incidence. Previous research indicates a connection between nasal MRSA colonization and subsequent clinical infections. A study by Dangerfield et al. (n > 400) specifically assessed nasal MRSA PCR as a predictor for HAP and VAP. This test demonstrated 88% sensitivity, 90.1% specificity, 35.4% positive predictive value, and a remarkable 99.2% negative predictive value (NPV)[8]. These findings were corroborated by subsequent publications, leading to the inclusion of nasal MRSA PCR in IDSA guidelines[8,34]. Consequently, a negative nasal MRSA swab can effectively guide the discontinuation of empirical MRSA therapy, leveraging its high NPV.
7. Syndromic panels provide a rapid etiological diagnosis for pneumonia by combining the detection of respiratory viruses with semi-quantitative bacterial pathogen identification. These panels can also identify pathogens not routinely recoverable by conventional culture, such as *Legionella pneumophila*, *Mycoplasma pneumoniae*, and *Chlamydia pneumoniae*. Furthermore, they offer valuable information on antibiotic resistance genes, facilitating early adjustments to treatment regimens.

However, limitations include incomplete pathogen coverage, the absence of comprehensive susceptibility data, higher costs, and the potential for false positives due to the detection of non-viable pathogen nucleic acids. Crucially, the semi-quantitative results (copies/ml) from these panels are not directly comparable to colony-forming units (CFU/ml) from cultures; panel values typically appear approximately one logarithm higher. Consequently, pathogens present at culture counts below routine reporting thresholds (e.g., $<10^4$ CFU/ml) might be reported as 10^5 copies/ml on panels, posing a risk of unnecessary antimicrobial use. Therefore, expert interpretation is paramount to mitigate this risk.

Given these considerations, syndromic panels do not replace conventional cultures[1]. Their implementation in hospitals should be aligned with an ASP to ensure proper result interpretation, timely reporting, and appropriate treatment. Adoption is also contingent on institutional resources and availability[12].

When it comes to laboratory testing of respiratory samples, the specific type of test requested should be guided by clinical suspicion. This includes considering whether a viral or bacterial etiology is suspected, or if unusual pathogens are a concern, as is often the case in immunocompromised patients. Below is a proposed algorithm for ordering specific tests on respiratory samples (Fig. 5).

Funding

No funding sources were required for this study.

Conflict of interest

None to declare.

Acknowledgments

The authors extend their gratitude to the following individuals for their invaluable content review and contributions to this document: Valeria Fabre, Associate Professor of Medicine at the Johns Hopkins University School of Medicine; Alejandra Corso and Fernando Pasteran from the Antimicrobial Service, National Reference Laboratory - ANLIS Dr. C. Malbrán, Argentina; and Rachel Smith, Twisha Patel, and Hanako Osuka from the Division of Healthcare Quality Promotion, National Center for Emerging and Zoonotic Infectious Diseases, U.S. Centers for Disease Control and Prevention (CDC).

References

1. Adams J, Ferguson K, Hirschy R, Konopka E, Meckel J, Benanti G, Kuhrau S, Albarillo F, Chang K, Santarossa M, Sapozhnikov J, Hoff B, Rech MA. Antimicrobial stewardship techniques for critically ill patients with pneumonia. Antibiotics (Basel). 2023;12:295.

2. Advani SD, North R, Turner NA, Ahmadi S, Denniss J, Francis A, Johnson R, Hasan A, Mirza F, Pardue S, Rao M, Rosshandler Y, Tang H, Schmader KE, Anderson DJ. Performance of urinalysis parameters in predicting urinary tract infection: does one size fit all? Clin Infect Dis. 2024;79:600–3.
3. Cilloniz C, Torres A, Niederman M. Management of pneumonia in critically ill patients. BMJ. 2021;375, e06587.
4. Coffey KC, Claeys K, Morgan DJ. Diagnostic stewardship for urine cultures. Infect Dis Clin North Am. 2024;38:255–66.
5. Cogliati Dezza F, Curtolo A, Volpicelli L, Ceccarelli G, Oliva A, Venditti M. Are follow-up blood cultures useful in the antimicrobial management of gram negative bacteremia? A reappraisal of their role based on current knowledge. Antibiotics (Basel). 2020;9:895.
6. Colgan R, Nicolle LE, McGlone A, Hooton TM. Asymptomatic bacteriuria in adults. Am Fam Physician. 2006;74:985–90.
7. Cornistein W, Colque AM, Staneloni MI, Lloria MM, Lares M, González AL, Fernández Garcés A, Carbone E. Neumonía asociada a ventilación mecánica. Actualización y recomendaciones inter-sociedades, Sociedad Argentina de Infectología – Sociedad Argentina de Terapia Intensiva. Medicina (B Aires). 2018;78:153–65.
8. Dangerfield B, Chung A, Webb B, Seville MT. Predictive value of methicillin-resistant *Staphylococcus aureus* (MRSA) nasal swab PCR assay for MRSA pneumonia. Antimicrob Agents Chemother. 2014;58:859–64.
9. Delgado V, Ajmone Marsan N, de Waha S, Bonaros N, Brida M, Burri H, Caselli S, Doenst T, Ederhy S, Erba PA, Foldager D, Fosbøl EL, Kovac J, Mestres CA, Miller OI, Miro JM, Pazdernik M, Pizzi MN, Quintana E, Rasmussen TB, Ristić AD, Rodés-Cabau J, Sionis A, Zühlke LJ, Borger MA, ESC Scientific Document Group. 2023 ESC Guidelines for the management of endocarditis. Eur Heart J. 2023;44:3948–4042 [erratum in: Eur Heart J. 2023 Dec 1;44(45):4780; erratum in: Eur Heart J. 2024 Jan 1;45(1):56; erratum in: Eur Heart J. 2025 Mar 13;46(11): 1082].
10. Doern GV, Carroll KC, Diekema DJ, Garey KW, Rupp ME, Weinstein MP, Sexton DJ. Practical guidance for clinical microbiology laboratories: a comprehensive update on the problem of blood culture contamination and a discussion of methods for addressing the problem. Clin Microbiol Rev. 2019;33, e00009-19.
11. Evans L, Rhodes A, Alhazzani W, Antonelli M, Coopersmith CM, French C, Machado FR, Mcintyre L, Ostermann M, Prescott HC, Schorr C, Simpson S, Wiersinga WJ, Alshamsi F, Angus DC, Arabi Y, Azevedo L, Beale R, Beilman G, Belley-Cote E, Burry L, Cecconi M, Centofanti J, Coz Yataco A, De Waele J, Dellinger RP, Doi K, Du B, Estenssoro E, Ferrer R, Gomersall C, Hodgson C, Møller MH, Iwashyna T, Jacob S, Kleinpell R, Klompas M, Koh Y, Kumar A, Kwizera A, Lobo S, Masur H, McGloughlin S, Mehta S, Mehta Y, Mer M, Nunnally M, Oczkowski S, Osborn T, Papathanassoglou E, Perner A, Puskarich M, Roberts J, Schweickert W, Seckel M, Sevransky J, Sprung CL, Welte T, Zimmerman J, Levy M. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. Intensive Care Med. 2021;47:1181–247.
12. Fabre V, Davis A, Diekema DJ, Granwehr B, Hayden MK, Lowe CF, Pfeiffer CD, Sick-Samuels AC, Sullivan KV, Van Schooneveld TC, Morgan DJ. Principles of diagnostic stewardship: a practical guide from the Society for Healthcare Epidemiology of America Diagnostic Stewardship Task Force. Infect Control Hosp Epidemiol. 2023;44:178–85.
13. Fabre V, Pleiss A, Klein E, Demko Z, Salinas A, Jones G, Gadala A, Hicks LA, Neuhauser MM, Srinivasan A, Cosgrove SE. A pilot study to evaluate the impact of a nurse-driven urine culture diagnostic stewardship intervention on urine cultures in the acute care setting. Jt Comm J Qual Patient Saf. 2020;46:650–5.
14. Fabre V, Sharara SL, Salinas AB, Carroll KC, Desai S, Cosgrove SE. Does this patient need blood cultures? A scoping review of indications for blood cultures in adult nonneutropenic inpatients. Clin Infect Dis. 2020;71:1339–47.
15. File TM Jr, Ramirez JA. Community-acquired pneumonia. N Engl J Med. 2023;389:632–41.
16. Fine MJ, Auble TE, Yealy DM, Hanusa BH, Weissfeld LA, Singer DE, Coley CM, Marrie TJ, Kapoor WN. A prediction rule to identify low-risk patients with community-acquired pneumonia. N Engl J Med. 1997;336:243–50.
17. Flores-Mireles A, Hreha TN, Hunstad DA. Pathophysiology treatment, and prevention of catheter-associated urinary tract infection. Top Spinal Cord Inj Rehabil. 2019;25:228–40.
18. Freifeld AG, Bow EJ, Sepkowitz KA, Boeckh MJ, Ito JI, Mullen CA, Raad II, Rolston KV, Young JA, Wingard JR. Infectious Diseases Society of America Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the Infectious Diseases Society of America. Clin Infect Dis. 2011;52:e56–93.
19. Gadsby NJ, Musher DM. The microbial etiology of community-acquired pneumonia in adults: from classical bacteriology to host transcriptional signatures. Clin Microbiol Rev. 2022;35, e0001522.
20. Hueth KD, Prinzi AM, Timbrook TT. Diagnostic stewardship as a team sport: interdisciplinary perspectives on improved implementation of interventions and effect measurement. Antibiotics (Basel). 2022;11:250.
21. Johns Hopkins Hospital. Department of Antimicrobial Stewardship Should I collect urine for bacterial culture? Algorithm for inpatients with or without a urethral catheter [Internet]. Baltimore: Johns Hopkins Hospital; 2020. Available from: https://www.hopkinsmedicine.org/-/media/antimicrobial-stewardship/urine-culture-algorithm.pdf. [Cited 1 July 2025].
22. Kalil AC, Metersky ML, Klompas M, Muscedere J, Sweeney DA, Palmer LB, Napolitano LM, O'Grady NP, Bartlett JG, Carratalà J, El Solh AA, Ewig S, Fey PD, File TM Jr, Restrepo MI, Roberts JA, Waterer GW, Cruse P, Knight SL, Brozek JL. 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;63:e61–111 [Epub 14 July 2016; erratum in: Clin Infect Dis. 2017 May 1;64(9):1298; erratum in: Clin Infect Dis. 2017 Oct 15;65(8):1435; erratum in: Clin Infect Dis. 2017 Nov 29;65(12):2161].
23. Kenaa B, Richert ME, Claeys KC, Shipper A, Sullivan KV, Schrank GM, O'Hara LM, Morgan DJ, Shanholtz C, Leekha S. Ventilator-associated pneumonia: diagnostic test stewardship and relevance of culturing practices. Curr Infect Dis Rep. 2019;21:50.
24. Kimura SI, Gomyo A, Hayakawa J, Tamaki M, Akahoshi Y, Harada N, Ugai T, Kusuda M, Kameda K, Wada H, Ishihara Y, Kawamura K, Sakamoto K, Sato M, Terasako-Saito K, Kikuchi M, Nakasone H, Kako S, Tanihara A, Kanda Y. Clinical significance of repeat blood cultures during febrile neutropenia in adult acute myeloid leukaemia patients undergoing intensive chemotherapy. Infect Dis (Lond). 2017;49:748–57.
25. Immunocompromised travelers.Kotton CN, Kroger AT, Freedman DO, Brunette GW, editors. CDC yellow book: health information for international travel 2026 [Internet]. Atlanta: Centers for Disease Control and Prevention (CDC); 2025. Available from: https://www.cdc.gov/yellow-book/hcp/travelers-with-additional-considerations/immunocompromised-travelers.html. [cited 1 July 2025].
26. Langford BJ, Amoah S, Hansen J, Hudd L, Almohri H, Wright J. BLADDER score: evaluating a tool to support urinary diagnostic and antibiotic stewardship in hospitalized adults. Infect Control Hosp Epidemiol. 2024;45:1–5.
27. Lorente L, Martín MM, Vidal P, Rebollo S, Ostabal MI, Solé-Violán J, Working Group on Catheter Related Infection Suspicion Management of GTEIS/SEMICYUC. Should central venous catheter

be systematically removed in patients with suspected catheter related infection? Crit Care. 2014;18:564.
28. Luna CM. Blood cultures in community-acquired pneumonia: are we ready to quit? Chest. 2003;123:977–8.
29. Macedo F, Nunes C, Ladeira K, Pinho F, Saraiva N, Bonito N, Pinto L, Gonçalves F. Antimicrobial therapy in palliative care: an overview. Support Care Cancer. 2018;26:1361–7.
30. Mahieu R, Lemarié C, Douillet D, Mercat A, Cormier H, Eveillard M, Dubée V, Riou J, Kouatchet A. Impact of a strategy based on unique blood culture sampling on contamination rate and detection of bloodstream infections in critically ill patients. Ann Intensive Care. 2023;13:13.
31. Mandell LA, Wunderink RG, Anzueto A, Bartlett JG, Campbell GD, Dean NC, Dowell SF, File TM Jr, Musher DM, Niederman MS, Torres A, Whitney CG, Infectious Diseases Society of America. American Thoracic Society Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis. 2007;44 Suppl. 2:S27–72.
32. Mermel LA, Allon M, Bouza E, Craven DE, Flynn P, O'Grady NP, Raad II, Rijnders BJ, Sherertz RJ, Warren DK. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 update by the Infectious Diseases Society of America. Clin Infect Dis. 2009;49:1–45 [erratum in: Clin Infect Dis. 2010 Apr 1;50(7):1079. Dosage error in article text. Erratum in: Clin Infect Dis. 2010 Feb 1;50(3):457].
33. Mermel LA, Rupp ME. Should blood cultures be drawn through an indwelling catheter? Open Forum Infect Dis. 2024;11, ofae248.
34. Metlay JP, Waterer GW, Long AC, Anzueto A, Brozek J, Crothers K, Cooley LA, Dean NC, Fine MJ, Flanders SA, Griffin MR, Metersky ML, Musher DM, Restrepo MI, Whitney CG. Diagnosis and treatment of adults with community-acquired pneumonia. An official clinical practice guideline of the American Thoracic Society and Infectious Diseases Society of America. Am J Respir Crit Care Med. 2019;200:e45–67.
35. Miller JM, Binnicker MJ, Campbell S, Carroll KC, Chapin KC, Gonzalez MD, Harrington A, Jerris RC, Kehl SC, Leal SM Jr, Patel R, Pritt BS, Richter SS, Robinson-Dunn B, Snyder JW, Telford S 3rd, Theel ES, Thomson RB Jr, Weinstein MP, Yao JD. Guide to utilization of the Microbiology Laboratory for Diagnosis of Infectious Diseases: 2024 update by the Infectious Diseases Society of America (IDSA) and the American Society for Microbiology (ASM). Clin Infect Dis. 2024;79:e1–154.
36. Morgan DJ, Malani P, Diekema DJ. Diagnostic stewardship-leveraging the laboratory to improve antimicrobial use. JAMA. 2017;318:607–8.
37. Nicolle LE, Gupta K, Bradley SF, Colgan R, DeMuri GP, Drekonja D, Eckert LO, Geerlings SE, Köves B, Hooton TM, Juthani-Mehta M, Knight SL, Saint S, Schaeffer AJ, Trautner B, Wullt B, Siemieniuk R. Clinical practice guideline for the management of asymptomatic bacteriuria: 2019 update by the Infectious Diseases Society of America. Clin Infect Dis. 2019;68:e83–110.
38. Papazian L, Klompas M, Luyt CE. Ventilator-associated pneumonia in adults: a narrative review. Intensive Care Med. 2020;46:888–906.
39. Pawlowicz A, Holland C, Zou B, Payton T, Tyndall JA, Allen B. Implementation of an evidence-based algorithm reduces blood culture overuse in an adult emergency department. Gen Int Med Clin Innov. 2016;1:20–5.
40. Quarton S, Livesey A, Pittaway H, Adiga A, Grudzinska F, McNally A, Dosanjh D, Sapey E, Parekh D. Clinical challenge of diagnosing non-ventilator hospital-acquired pneumonia and identifying causative pathogens: a narrative review. J Hosp Infect. 2024;149:189–200.
41. Schoffelen T, Papan C, Carrara E, Eljaaly K, Paul M, Keuleyan E, Martin Quirós A, Peiffer-Smadja N, Palos C, May L, Pulia M, Beovic B, Batard E, Resman F, Hulscher M, Schouten J, ESCMID Study Group for Antimicrobial Stewardship (ESGAP). European society of clinical microbiology and infectious diseases guidelines for antimicrobial stewardship in emergency departments (endorsed by European association of hospital pharmacists). Clin Microbiol Infect. 2024;30:1384–407.
42. Simões AS, Couto I, Toscano C, Gonçalves E, Póvoa P, Viveiros M, Lapão LV. Prevention and control of antimicrobial resistant healthcare-associated infections: the microbiology laboratory rocks! Front Microbiol. 2016;7:855.
43. So B, Kim J, Jo JK, So H. Recent developments in preventing catheter-related infections based on biofilms: a comprehensive review. Biomicrofluidics. 2024;18, 051506.
44. Srzić I, Nesek Adam V, Tunjić Pejak D. Sepsis definition: what's new in the treatment guidelines. Acta Clin Croat. 2022;61 Suppl. 1:67–72.
45. Torres A, Niederman MS, Chastre J, Ewig S, Fernandez-Vandellos P, Hanberger H, Kollef M, Li Bassi G, Luna CM, Martin-Loeches I, Paiva JA, Read RC, Rigau D, Timsit JF, Welte T, Wunderink R. International ERS/ESICM/ESCMID/ALAT guidelines for the management of hospital-acquired pneumonia and ventilator-associated pneumonia: 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). Eur Respir J. 2017;50, 1700582.
46. Trautner BW, Grigoryan L, Petersen NJ, Hysong S, Cadena J, Patterson JE, Naik AD. Effectiveness of an antimicrobial stewardship approach for urinary catheter-associated asymptomatic bacteriuria. JAMA Intern Med. 2015;175:1120–7.
47. Ulrich P, Lepak AJ, Chen DJ. Diagnostic and therapeutic utility of positive intravascular catheter tip cultures. Microbiol Spectr. 2022;10, e0402222.
48. Van Goethem S, Boogaerts H, Cuykx M, van den Bremen P, Wouters K, Goossens H, Jansens H, Ten Kate GL. Follow-up blood cultures in *Staphylococcus aureus* bacteremia: a probability-based optimization. Eur J Clin Microbiol Infect Dis. 2022;41:1263–8.
49. Vaughn VM, Dickson RP, Horowitz JK, Flanders SA. Community-acquired pneumonia: a review. JAMA. 2024;332:1282–95.
50. Velasco M, Martínez JA, Moreno-Martínez A, Horcajada JP, Ruiz J, Barranco M, Almela M, Vila J, Mensa J. Blood cultures for women with uncomplicated acute pyelonephritis: are they necessary? Clin Infect Dis. 2003;37:1127–30.