AMERICAN THORACIC SOCIETY DOCUMENTS

Diagnosis and Management of Community-acquired Pneumonia
An Official American Thoracic Society Clinical Practice Guideline

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Abstract

Background: Understanding of the diagnosis and treatment of adults with community-acquired pneumonia (CAP) has evolved thanks to new evidence, experience, and emerging technologies. This document updates evidence-based clinical practice guidelines on four key questions for the diagnosis and management of adult patients with CAP.

Methods: A multidisciplinary panel integrated systematic reviews of comparative evidence with other relevant research and clinical experience, then applied Grading of Recommendations, Assessment, Development and Evaluation methodology to produce recommendations using the Evidence to Decision Framework.

Results: The panel formulated clinical recommendations that address questions related to CAP, including lung ultrasound for diagnosis, empiric antibacterial therapy if a test result for a respiratory virus is positive, antibiotic duration, and the use of systemic corticosteroids.

Conclusions: The panel formulated and provided the rationale for recommendations on selected diagnostic and treatment strategies for adult patients with CAP.

Keywords: pneumonia; lower respiratory tract infection; practice guidelines; guideline update

Summary of Recommendations

1. Lung ultrasound versus chest radiography to diagnose CAP
For adults with suspected CAP, we suggest lung ultrasound is an acceptable diagnostic alternative to chest radiography in medical centers where appropriate clinical expertise exists (conditional recommendation, low-quality evidence). Vote: 13 (87%) of 15 committee members voted in favor of this recommendation.
2. Empiric antibacterial therapy for CAP with positive respiratory virus testing
For adult outpatients without comorbidities who have clinical and

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A data supplement for this document is available via the Supplements tab at the top of the online article.

Artificial Intelligence Disclaimer: No artificial intelligence tools were used in writing this manuscript.

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imaging evidence of CAP and who have a positive test result for a respiratory virus, we suggest not prescribing empiric antibiotics (conditional recommendation, very low-quality evidence). Remark: This is a conditional recommendation because the balance between benefit and harm of empiric antibiotics will vary on the basis of clinical context (*see* Table 1). Vote: 14 (93%) of 15 committee members voted in favor of not prescribing antibiotics.

For adult outpatients with comorbidities who have clinical and imaging evidence of CAP and who have a positive test result for a respiratory virus, we suggest prescribing empiric antibiotics because of concern for bacterial-viral coinfection (conditional recommendation, very low-quality evidence). Remark: This is a conditional recommendation because the balance between benefit and harm of empiric antibiotics will vary on the basis of clinical context (*see* Table 1). Vote: 11 (73%) of 15 committee members voted in favor of prescribing antibiotics.

For adult inpatients with clinical and imaging evidence of nonsevere CAP who have a positive test result for a respiratory virus, we suggest prescribing empiric antibiotics because of concern for bacterial-viral coinfection (conditional recommendation, very low-quality evidence). Remark: This is a conditional recommendation because the balance between benefit and harm of empiric antibiotics will vary on the basis of clinical context (Table 1). Vote: 12 (80%) of 15 committee members voted in favor of prescribing antibiotics.

For adult inpatients with clinical and imaging evidence of severe CAP who have a positive test result for a respiratory virus, we suggest prescribing empiric antibiotics because of concern for bacterial-viral coinfection (conditional recommendation, very low-quality evidence). Remark: Although the committee was unanimous in making this recommendation, this is a conditional recommendation because of the absence of comparative evidence. Vote: 15 (100%) of 15 committee members voted in favor of prescribing antibiotics.

3. Antibiotic duration for CAP

For adult outpatients with CAP who reach clinical stability, we suggest less than 5 days of antibiotics (minimum of 3-d duration) rather than 5 or more days of antibiotics (conditional recommendation, low-quality evidence). Remark: This is a conditional recommendation that requires individualization. *See* Table 1 for factors that weaken this recommendation. Vote: 15 (94%) of 16 committee members voted in favor of less than 5 days of antibiotics.

For adult inpatients with nonsevere CAP who reach clinical stability, we suggest less than 5 days of antibiotics (minimum of 3-d duration) rather than 5 or more days of antibiotics (conditional recommendation, low-quality evidence). Remark: This is a conditional recommendation that requires individualization. *See* Table 1 for factors that weaken this recommendation. Vote: 11 (69%) of 16 committee members voted in favor of less than 5 days of antibiotics.

For adult inpatients with severe CAP who reach clinical stability, we suggest 5 or more days of antibiotics rather than less than 5 days of antibiotics (strong recommendation, low-quality evidence). Remark: This recommendation is strong despite the low-quality of evidence because insufficient antibiotic therapy can result in serious adverse outcomes or death in patients with severe CAP. Vote: 15 (94%) of 16 committee members voted in favor of 5 or more days of antibiotics.

4. Systemic corticosteroids for CAP

For adult inpatients with nonsevere CAP, we recommend NOT administering systemic corticosteroids (strong recommendation, low-quality evidence). Remark: This recommendation is strong because, although the overall quality of evidence was low, the intent is to avoid harmful side effects such as hyperglycemia for which there is robust evidence. Vote: 16 (100%) of 16 committee members voted in favor not administering systemic corticosteroids.

For adult inpatients with severe CAP, we suggest systemic corticosteroids (conditional recommendation, low-quality evidence). Remark: This recommendation excludes patients with severe CAP caused by influenza pneumonia. Vote: 15 (94%) of 16 committee members voted in favor systemic corticosteroids.

Introduction

In 2019, the American Thoracic Society (ATS) and the Infectious Diseases Society of America (IDSA) provided evidence-based

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Table 1. Individual Patient Factors to Consider that May Strengthen or Weaken Recommendations

Recommendation	Strength and Evidence Quality	Factors that Strengthen the Recommendation	Factors that Weaken the Recommendation
1. Lung ultrasound versus chest radiography to diagnose CAP			
For adults with suspected CAP, we suggest LUS is an acceptable diagnostic alternative to chest radiography in medical centers where appropriate clinical expertise exists.	Conditional Low-quality evidence 94% consensus	All criteria for establishing expertise met (Table 4) No availability of chest radiography (LUS as alternative to radiography) High patient risks or cost of CT scan (LUS as alternative to CT) Patient convenience and radiation exposure compared with chest radiography and CT	Not all criteria for establishing expertise met (Table 4) Suspicion of alternative/additional diagnoses (pulmonary embolism, malignancy) Barriers to high-quality LUS (obesity, drains, scars, wounds, difficulty holding position)
2. Empiric antibacterial therapy for CAP with positive respiratory virus testing			
For adult outpatients without comorbidities who have clinical and imaging evidence of CAP and who have positive test result for a respiratory virus, we suggest not prescribing empiric antibiotics.	Conditional Very low-quality evidence 93% consensus	Low suspicion for bacterial coinfection (clinical history, low/normal inflammatory markers, clinical history, radiologic findings suggestive of viral etiology, viral pathogen with low prevalence of bacterial codetection) Higher risk of harm from antibiotic exposure (history of *Clostridioides difficile*, severe antibiotic allergy or adverse event) Patient preference to avoid antibiotic exposure	Suspicion of bacterial coinfection (long symptom onset, "double sickening," purulent sputum, elevated inflammatory markers, radiologic findings such as consolidative infiltrate, viral pathogen with high prevalence of bacterial codetection, exposure to *Mycoplasma pneumoniae*) High risk of harm if missed bacterial infection (elderly, pregnant, signs/symptoms suggestive of more severe illness) Barriers to follow-up or communication
For adult outpatients with comorbidities who have clinical and imaging evidence of CAP and who have positive test result for a respiratory virus, we suggest prescribing empiric antibiotics because of concern for bacterial-viral coinfection.	Conditional Very low-quality evidence 73% consensus	Suspicion of bacterial coinfection (long symptom onset, "double sickening," purulent sputum, elevated or increasing inflammatory markers, radiologic findings such as consolidative infiltrate) Low likelihood that virus identified explains etiology and severity of pneumonia (i.e., virus with low virulence or high risk of coinfection) High risk of harm if missed bacterial infection High illness severity, severe symptoms Higher number, severe, or poorly controlled comorbidities	Low suspicion of bacterial infection (clinical history, normal inflammatory markers, radiologic findings suggestive of viral etiology) High likelihood that virus identified explains etiology and severity of pneumonia (virus with high virulence, low risk of coinfection) Lower risk of harm if missed bacterial infection Lower illness severity Single, mild, or well-controlled comorbidities Higher risk of harm from antibiotic exposure (History of *C. difficile,* antibiotic allergy/adverse event) Patient preference to avoid antibiotic exposure
For adult inpatients with clinical and imaging evidence of nonsevere CAP who have positive test result for a respiratory virus, we suggest prescribing empiric antibiotics because of concern for bacterial-viral coinfection.	Conditional Very low-quality evidence 80% consensus	Same as above	Same as above
For adult inpatients with clinical and imaging evidence of severe CAP who have positive test result for a respiratory virus, we suggest prescribing antibiotics because of concern for bacterial-viral coinfection	Conditional Very low-quality evidence 100% consensus	Sepsis, severe respiratory failure, elevated or increasing inflammatory markers Chest radiograph showing consolidation infiltrates	Higher risk of harm from antibiotic exposure (history of *C. difficile*, antibiotic allergy, or antibiotic adverse event)

(*Continued*)

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Table 1. (*Continued*)

Recommendation	Strength and Evidence Quality	Factors that Strengthen the Recommendation	Factors that Weaken the Recommendation
3. Antibiotic duration for CAP			
For adult outpatients with CAP who reach clinical stability*, we suggest less than 5 days of antibiotics (minimum of 3-d duration) rather than 5 or more days of antibiotics.	Conditional Low-quality evidence 94% consensus	Higher risk of harm from prolonged antibiotic exposure (history of *C. difficile* or an antibiotic adverse event) Patient preference to minimize antibiotic exposure	Barriers to self-assessment, follow-up, or communication to ensure recovery Organism requiring longer duration (i.e., *Staphylococcus aureus*, *Pseudomonas aeruginosa*, suspected *Legionella pneumophila* or other intracellular microorganisms)† Radiographic findings (high burden of disease, necrotizing process, dense consolidations) Underlying lung disease (e.g., bronchiectasis, postobstructive pneumonia, chronic respiratory insufficiency†) Recent hospitalization or resident in long-term care facility†
For adult inpatients with nonsevere CAP who reach clinical stability*, we suggest less than 5 days of antibiotics (minimum of 3-d duration) rather than 5 or more days of antibiotics.	Conditional Low-quality evidence 69% consensus	Patient preference to minimize antibiotic exposure Resolution of inflammatory markers	Organism requiring longer duration (i.e., *Staphylococcus aureus*, *Pseudomonas aeruginosa*, suspected *Legionella pneumophila* or other intracellular microorganisms)† Pneumonia complication (e.g., empyema/parapneumonic effusion, abscess/necrotizing process, bacteremia, extrapulmonary infection) Underlying lung disease (e.g., bronchiectasis, postobstructive pneumonia, chronic hypoxemia†) Pregnancy, recent antibiotics† Recent hospitalization or resident in long-term care facility†
For adult inpatients with severe CAP who reach clinical stability, we suggest 5 or more days of antibiotics rather than less than 5 days of antibiotics.	Strong Low-quality evidence 100% consensus	—	—
4. Corticosteroids			
For adult inpatients with nonsevere CAP, we recommend NOT administering systemic corticosteroids‡	Strong Low-quality evidence 100% consensus	—	—
For adult inpatients with severe CAP, we suggest systemic corticosteroids.	Conditional Low-quality evidence 94% consensus	Short time interval between symptom onset and presentation Ability to administer corticosteroids early after meeting criteria for severe CAP (within 24 h) ICU admitted Respiratory failure (Pa_{O_2}/FI_{O_2} ratio <300) Elevated inflammatory markers (i.e., CRP, IL-6)	Longer time between symptom onset and presentation Longer time since onset of severe CAP (e.g., >72 h) Lack of respiratory failure Normal or low inflammatory markers Contraindications to corticosteroids (i.e., influenza, *Aspergillus*, uncontrolled diabetes, recent gastrointestinal bleeding) Pregnancy†

Definition of abbreviations: CAP = community-acquired pneumonia; CRP = C-reactive protein; CT = computed tomography; LUS = lung ultrasound.
Factors listed in this table were generated from clinical experience, observational studies, and pathophysiologic rationale but are not supported by high-quality comparative evidence and should be integrated with clinical judgment for individual patient care. Recommendations are not for patients with immunocompromise. See other guidelines focused on this patient population.
*The duration of antibiotics should be determined on the basis of daily assessment of clinical stability.
†Exclusion criteria from key studies.
‡Recommendation and factors listed are for patients without another established indication of corticosteroids.

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practice guidelines on the management of adult patients with community-acquired pneumonia (CAP) to provide an update to the previous 2007 guideline (1, 2). It addressed 16 specific areas for recommendations surrounding diagnostic testing, determination of site of care, selection of empiric antibiotic therapy, and subsequent management decisions. Since publication of the 2019 guidelines, the care of CAP has been impacted by the COVID-19 pandemic and the availability of rapid molecular tests for multiple pathogens, including viruses, emerging imaging technology, and new evidence surrounding the host response and the potential role of corticosteroids. Given the dynamic nature of the evidence base for CAP and the need for more rapidly updated guidance, there has been a move toward more rapidly generated incremental guideline recommendation updates. The first of these updates addressed nucleic acid testing for noninfluenza and non–SARS-CoV-2 viruses (3). The present update addresses four clinically relevant questions, of which two are updates from the 2019 guideline and two are new questions:

1. Should lung ultrasound be considered a reasonable alternative to chest radiography for diagnosis in adults with suspected community-acquired pneumonia? (New)
2. Should adults with community-acquired pneumonia who have a positive test result for a respiratory virus be treated with empiric antibacterial therapy? (New)
3. Should adults with community-acquired pneumonia who reach clinical stability be treated with less than 5 days of antibiotics? (Update from 2019)
4. Should adults who are hospitalized with community-acquired pneumonia be treated with corticosteroids? (Update from 2019)

This guideline update addresses CAP in immunocompetent adult patients. Pneumonia is a lower respiratory tract infection (LRTI) that causes inflammation in the alveoli. CAP is acquired outside of hospital or healthcare settings, and most commonly patients present to the emergency department or primary care. Because CAP cannot be clinically distinguished from other LRTIs without chest imaging to confirm alveolar inflammation, the standard diagnosis of CAP requires clinical signs and symptoms plus chest imaging confirmation to visualize alveolar inflammation. This guideline update focuses only on those patients with a standard diagnosis of CAP.

CAP can be caused by bacterial, viral, or fungal pathogens or a combination of pathogens. The diagnosis does not require microbiologic confirmation, because microbiologic tests have poor sensitivity. This definition includes all viruses, including SARS-CoV-2. However, this guideline update does not address the syndrome of SARS-CoV-2 pneumonia that was seen during the COVID-19 pandemic. Patients who presented with pneumonia caused by SARS-CoV-2 during the COVID-19 pandemic exhibited distinct patterns of presentation and responses to therapies because of its novelty, virulence, dominance over other pathogens, and naivety of the host immune system. Evidence and guidelines were generated to support management (4, 5) that are distinct from this guideline and do not apply to CAP. With the exception of the lung ultrasound (LUS) question, none of the other formal evidence reviews included studies conducted during the pandemic. As we emerge from the pandemic and SARS-CoV-2 becomes integrated into the milieu of respiratory pathogens that cause CAP, we expect the pattern of presentation, epidemiology, and responsiveness to therapy for patients with CAP caused by SARS-CoV-2 to change. At the time of this publication, it is not clear whether today's patient with pneumonia caused by SARS-CoV-2 would most benefit from standard CAP management or COVID-19 treatments used during the pandemic.

This guideline update is also not intended for use in immunocompromised hosts (ICHs). Patients classified as ICHs have compromised immune systems because of certain medical conditions, including malignancy, advanced HIV infection, and organ transplant, and treatments that impair the immune system, including chronic glucocorticoids, chemotherapy, conventional disease-modifying antirheumatic drugs, and biological agents used to treat various rheumatologic, dermatologic, gastrointestinal, and autoimmune disorders. The clinical presentation, pathogen profile, and host responses to pneumonia in ICHs are markedly different from those in nonimmunocompromised individuals. For detailed guidance on the diagnosis and management of pneumonia in ICHs, please consult specific recommendations provided by the ATS and other medical organizations (6, 7).

The understanding of CAP is evolving. Previously considered a sterile compartment, the lung is now understood as an active ecosystem with organisms that interact with each other and host cells in complex, dynamic ways (8). Pneumonia is no longer considered a simple matter of invasion of a sterile space by a foreign organism with the simple solution of eliminating offending pathogens. Rather, it is a state that emerges from structural and functional host susceptibility, dysbiosis (an imbalance in microbial populations), inflammation from a dysregulated host response, and tissue damage (9). This evolving understanding of the microbiology and host response of CAP has important implications for clinical management, particularly surrounding the optimal use of diagnostic tests, antimicrobials, and host modulating therapies. As a result, clinicians need to pursue more individualized, tailored approaches to clinical management.

We have maintained the convention of separate recommendations based on setting and severity of illness similar to prior ATS/IDSA guidelines: outpatients, inpatients with nonsevere CAP, and inpatients with severe CAP as defined by previously validated criteria (Table 2). However, decisions about site of care may be based on considerations other than severity and can vary widely between hospitals and practice sites. These guidelines are intended not to impose a standard of care based on singular categories but to provide the basis for rational decisions in the management of patients with CAP. The majority of the recommendations in this guideline update are conditional, meaning that a sizable minority of patients may not want the suggested course of action, and clinicians must help patients arrive at a management decision consistent with their values and preferences (Table 3). For each guideline recommendation, the committee generated patient factors to consider that strengthen or weaken the recommendation (Table 1). Clinicians should review these factors and individualize recommendations on the basis of their assessment of how well the guidelines apply to their patient. Clinicians, patients, third-party payers, institutional review committees, other stakeholders, and courts should never view or use these

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Table 2. 2007 and 2019 Infectious Diseases Society of America/American Thoracic Society Criteria for Defining Severe Community-acquired Pneumonia

Validated definition includes either one major criterion or three or more minor criteria
Major criteria
Septic shock with need for vasopressors
Respiratory failure requiring mechanical ventilation
Minor criteria
Respiratory rate ⩾30 breaths/min
$Pa_{O_2}/F_{I_{O_2}}$ ratio ⩽250
Multilobar infiltrates
Confusion/disorientation
Uremia (blood urea nitrogen concentration, ⩾20 mg/dl)
Leukopenia (white blood cell count, <4,000 cells/μl)
Thrombocytopenia (platelet count, <100,000/μl)
Hypothermia (core temperature, <36°C)
Hypotension requiring aggressive fluid resuscitation

recommendations as mandates. No guideline or recommendation can account for all the unique individual clinical circumstances that must be considered in medical decision making. Therefore, no one responsible for evaluating clinicians' actions should attempt to apply the recommendations from these guidelines by rote or in a blanket fashion. Statements about underlying values and preferences, as well as qualifying remarks, accompanying each recommendation are integral parts that serve to facilitate nuanced interpretation. They should never be omitted when quoting or translating recommendations from these guidelines.

Methods

A multidisciplinary (pulmonology, infectious disease, internal medicine, critical care, hospital medicine, emergency medicine, and evidence synthesis) panel of nine experts from the ATS and nine from the IDSA was composed to identify clinically important interventions for CAP that warrant review of the evidence. In accordance with Institute of Medicine (now the National Academy of Medicine) standards, clinical questions were posed, and systematic reviews of comparative effectiveness studies published between January 1, 1946, and March 31, 2023, were performed by four members of the methodology team to inform recommendations (10, 11). The literature search was updated on November 27, 2024, and February 20, 2025, with an additional 60 articles reviewed by the methodology team and cochairs. No studies were identified that required insertion into the completed systematic reviews. When the comparative evidence alone was deemed insufficient to inform a recommendation, it was supplemented with epidemiological evidence, clinical observations, and disease pathophysiology. The Grading of Recommendations, Assessment, Development and Evaluation approach was employed to formulate and rate the recommendations (12). The Convergence of Opinion on Recommendations and Evidence process was used to help generate consensus (13). To integrate patient feedback, the document was reviewed independently by two patient representatives (M.P. and C.H.), who were identified and recruited by committee members through nontherapeutic relationships for their experiences with having CAP. Each patient representative provided feedback surrounding each recommendation via a virtual meeting facilitated by the ATS senior director of documents and patient education, Judy Corn. Targeted questions for each recommendation prepared by cochairs were also answered. Feedback was then incorporated throughout the document by chairs and patient representatives and summarized in the patient input statement.

The guideline underwent anonymous peer review by 15 content experts (4 from the ATS and 11 from the IDSA). Following multiple cycles of review and revision, the guideline was reviewed and approved by a multidisciplinary board of directors from the ATS. However, it was not approved by the IDSA. The guideline update will be reviewed by the ATS 3 years after publication, and it will be determined if updating is necessary.

Table 3. Strength of Recommendations

	Strong Recommendation ("We recommend . . .")	Conditional Recommendation ("We suggest . . .")
For patients	The overwhelming majority of individuals in this situation would want the recommended course of action, and only a small minority would not.	The majority individuals in this situation would want the suggested course of action, but a sizable minority would not.
For clinicians	The overwhelming majority of individuals should receive the recommended course of action. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator. Formal decision aids are not likely to be needed to help individuals make decisions consistent with patient values and preferences.	Different choices will be appropriate for different patients, and you must help each patient arrive at a management decision consistent with her or his values and preferences. Decision aids may be useful to help individuals make decisions consistent with their values and preferences. Clinicians should expect to spend more time with patients when working toward a decision.
For policy makers	The recommendation can be adapted as policy in most situations, including for use as performance indicators if supported by high- or moderate-quality evidence.	Policy making will require substantial debates and involvement of many stakeholders. Policies are also more likely to vary between regions. Performance indicators would have to focus on the fact that adequate deliberation about the management options has taken place.

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A detailed description of the methods is provided in the online supplement. Implications of the strengths of the recommendations (i.e., strong vs. conditional) are described in Table 3.

Question 1: Should Lung Ultrasound Be Considered a Reasonable Diagnostic Alternative to Chest Radiography in Adults with Suspected Community-acquired Pneumonia?

Rationale. The diagnosis of pneumonia carries substantial uncertainty (14). Because signs and symptoms are neither sensitive nor specific, it is essential to confirm the clinical suspicion of pneumonia with visualization of alveolar inflammation on imaging. Confirming pneumonia through chest imaging is thus a standard in settings in which it is available, because the remainder of evidence-based practice hinges on diagnosis.

Chest radiography, which is the most common way of documenting a diagnosis, is less accurate than chest computed tomography (CT). However, chest CT is more costly and time-consuming. Both of these modalities require a radiology department. An estimated two-thirds of the world's population has limited or no access to radiographic imaging (15), and past clinical trials on pneumonia have been limited to use of chest radiography or CT (16, 17), effectively excluding much of the world from clinical research, the evidence base, and high-quality diagnosis.

Since the 1990s, studies of LUS have shown that this technique can accurately detect common lung pathologies when performed by clinicians competent in its use (16, 17). In recent years, more clinicians have begun using LUS to diagnose and manage patients with pulmonary disease thanks to advancements in ultrasound (US) technology, increased availability of portable US machines, and integration of training in LUS in undergraduate and graduate medical education (18, 19). Although our historical standard of diagnosis in CAP has been chest radiography (radiography or CT), there are currently few studies and guideline recommendations in this area. Because of the emerging evidence and availability of LUS, we pursued a review of the evidence surrounding LUS for the diagnosis of CAP.

Evidence synthesis. The guideline committee *a priori* defined three outcomes as "critical": *1*) time to appropriate diagnosis, treatment, and disposition; *2*) repeat visits to emergency department, clinic, or hospital; and *3*) test accuracy. The committee also *a priori* defined four outcomes as "important": use of advanced imaging, cost, and provider and patient experience (i.e., satisfaction).

We identified no studies that measured any outcomes besides accuracy when comparing LUS with chest radiography in patients with suspected CAP. No studies directly compared the effects of LUS and chest radiography on clinical outcomes in patients with suspicion for CAP. However, 12 studies of patients who underwent LUS and chest radiography and then proceeded to chest CT for clinical reasons (including discordance between LUS and radiography) were identified, which examined the test characteristics of LUS and chest radiography using chest CT as the reference standard (20–31) (*see* Table E1 in the online supplement). These studies provided indirect evidence, because they included only a subset of patients with suspected CAP, specifically those who also required a chest CT scan.

One study was judged to be an outlier because of nearly 100% discordance between US and chest radiography and was excluded (31). Thus, 11 studies with 939 patients were included (20–30). When the data were aggregated by meta-analysis, LUS had a median sensitivity of 95% (range, 68–100%), whereas chest radiography had a median sensitivity of 70% (range, 16–94%). The median specificity of US was 75% (range, 0–100%), whereas the median specificity of chest radiography was 55% (range, 0–94%) (Figure E2, Table E2).

Overall, the committee's certainty in the accuracy of the test characteristics (the quality of evidence) for both LUS and chest radiographs was judged to be low because of inconsistency (wide range of estimates across studies) and imprecision (confidence intervals [CIs] were wide with the ends leading to different clinical actions). The committee acknowledged the indirectness of the population described above but did not downgrade for it, because the committee concluded that it did not further diminish confidence in the estimated effects (Table E2).

Committee's discussion. Because the existing studies were indirect, inconsistent, and imprecise and lacked clinical outcome evaluations, the true clinical performance of LUS for the diagnosis of CAP is uncertain. There remains substantial uncertainty surrounding whether LUS is equivalent to chest radiography for management or which diagnostic approach for pneumonia results in the best outcomes for patients. However, our evidence synthesis suggests that LUS is likely to be at least as accurate as chest radiography in confirming a clinical suspicion of pneumonia. Thus, although we acknowledge the evidence is of low quality, we conditionally suggest that LUS is an acceptable diagnostic alternative to chest radiography when performed by clinicians and in settings with adequate expertise.

The studies included in the meta-analysis were limited to an indirect population: patients with indications for chest CT rather than all patients with clinical suspicion for CAP. One of the indications for chest CT is a negative chest radiography finding in a patient with high clinical suspicion of pneumonia. Interpreting the performance characteristics found in these studies should be done with extreme caution, because they are likely not generalizable to the broader population of patients with clinical suspicion of CAP. In practice, we might expect more similar performance characteristics between the two diagnostic tests, because a larger proportion of cases would have concordant findings between chest radiography and LUS. Thus, the accuracy of LUS compared with chest radiography in the population of patients with clinical suspicion for CAP is yet to be determined.

The skill of the ecographer and the quality of the US image are paramount to ensuring an accurate diagnosis. In contrast to traditional imaging studies performed by technicians and interpreted by radiologists, LUS can be performed as a point-of-care US application by bedside clinicians to answer a focused set of clinical questions. Clinicians must demonstrate the skills to identify the most common sonographic features of pneumonia, including consolidation (irregular marginal contour, air bronchogram, the air trapping sign), vertical artifacts (B-lines), and the presence of pleural effusion. Other important factors impacting LUS accuracy include the protocol followed, region of focus, and patient factors, such as obesity, drains, scars, wounds, and movement. Although full recommendations surrounding training are beyond the scope of this guideline, clinician skill level must be formally assessed to ensure that the quality of the images acquired matches the quality in published studies. Standard protocols must be followed and documented. LUS results should also be stored and reported within the

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Table 4. Key Criteria for Establishing Expertise in Lung Ultrasound Examinations

Factor	Requirements
Ultrasound equipment	Either a cart-based or handheld ultrasound device with a low-frequency ultrasound probe that provides adequate penetration, typically 14–16 cm in adults, is needed to assess for pneumonia.
Training	Requisite training in LUS must provide background knowledge; practice in image acquisition, optimization, and interpretation; and knowledge of clinical integration. Mastery of LUS knowledge and skills through formal assessments should be demonstrated before use in clinical practice as recommended by specialty guidelines (138–141).
Imaging protocol	A standardized protocol evaluating the superior and inferior portions of the anterior, lateral, and posterior chest wall should be used (32).
Image archive	Dynamic ultrasound images, typically 2–4-s video loops, should be recorded, labeled per local convention, and saved in a retrievable image archive.
Documentation	Documentation of the operator, indications, examination performed, and ultrasound findings of the pleura and lung parenchyma, including location of abnormalities using standard terminology, should be included as a report within the patient's medical record.
	Findings from different imaging modalities shall be compared and periodic quality assurance checks of clinicians using LUS should be performed at the same level of radiologic images. Discrepancies of imaging findings associated with negative outcomes should be reviewed for quality improvement.
Patient	Patient factors that limit LUS imaging, including obesity, drains, scars, wounds, and uncooperativeness, should be considered when choosing imaging modality.

Definition of abbreviation: LUS = lung ultrasound.

medical record with the same standards as those of radiographic images and reports to allow others to review and for longitudinal comparisons. Table 4 summarizes important criteria to ensure high-quality LUS in practice.

This recommendation has different implications for different settings and patients. *See* Table 1 for additional patient factors to consider that strengthen or weaken this recommendation. For settings in which and patients for whom chest radiography is available, LUS may serve as an alternative diagnostic tool if clinical suspicion of pneumonia is high, a chest radiograph finding is negative, and there are barriers or contraindications to a timely diagnosis with CT such as patient safety or cost. For settings in which and patients for whom chest radiography is not an option (due to either lack of radiology services, cost, or other patient concerns including radiation exposure and convenience), LUS is an important advance to clinical diagnosis, enabling the clinician to diagnose CAP more accurately. LUS also has distinct strengths and weaknesses relative to chest radiography. Compared with radiography, lung ultrasound is smaller, does not require technicians and supplies, and allows a focused visualization of the pleural space, which could be important advantages. However, LUS may not be appropriate for patients in whom it is important to visualize the entire lung or rule out additional processes that can be visualized only by radiography (Table 1).

Recommendation. For adults with suspected CAP, we suggest that LUS is an acceptable diagnostic alternative to chest radiography in settings where the appropriate expertise exists (conditional recommendation, low-quality evidence). Vote: 13 (87%) of 15 committee members voted in favor of a conditional recommendation for considering LUS as an acceptable diagnostic alternative to chest radiography.

What others are saying. Several professional and specialty societies have published clinical practice guidelines and recommendations to standardize the use of LUS for multiple conditions (32–40). International evidence-based recommendations for point-of-care LUS published in 2012 suggested the use of LUS for the diagnosis of pneumonia based on an evidence synthesis of diagnostic accuracy compared with chest radiography (32).

Research needs. Our recommendation is conditional based on low-quality evidence because of a lack of studies that have *1*) included the entire population of patients with suspected CAP and *2*) assessed the performance of LUS in clinical practice and its impact on outcomes compared with chest radiography diagnosis. There are several unanswered questions surrounding the clinical approach to pneumonia diagnosis, particularly surrounding the choice of imaging or how to interpret discordant results. Two types of studies are needed to improve the evidence supporting this recommendation: *1*) well-performed, multisite diagnostic accuracy studies that include all patients with clinical suspicion of pneumonia, ideally at diverse settings in patients with a broad range of illness severity; and *2*) randomized clinical trials that directly compare the impact of different imaging approaches to the diagnosis of pneumonia, including LUS, chest radiography, and chest CT, on management and clinical outcomes, cost, and patient and provider experience.

Question 2: Should Adults with Community-acquired Pneumonia Who Have a Positive Test Result for a Respiratory Virus Be Treated with Empiric Antibacterial Therapy?

Rationale. The decision whether to administer empiric antibacterial therapy to a patient with pneumonia who has a positive test result for a virus is difficult. The question should be interpreted not as whether to treat viruses with antibiotics (which have no effect on viral infections) but when to consider the risks and consequences of viral-bacterial coinfection. The lung compartment is difficult to sample directly, and microbiology cultures take time to grow and can be inaccurate. The important role of bacteria in deaths caused by influenza was established by Morens and colleagues (41), who found evidence for coinfecting bacteria in lung

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tissue from more than 90% of persons who died in the 1918–1919 influenza epidemic. *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Staphylococcus aureus*, and *Haemophilus influenzae* are the most common bacterial pathogens identified in patients with influenza virus coinfection (42). In the 1957–1958 Asian influenza outbreak, coinfection with *S. aureus* was the major cause of death (43). Although the mechanisms leading to bacterial-viral coinfection are unclear, proposed theories include viral infection first causing epithelial barrier compromise, impaired immunity, and inflammation producing enriched nutrients, providing an opportunity for bacterial overgrowth (44, 45). Because of poor sensitivity of microbiology and concern for coinfection, empiric antibiotics have historically been administered, regardless of whether a pathogen is identified. However, the widespread availability of rapid molecular assays has unearthed more viral pathogens, as well as codetection of viral with bacterial pathogens, than previously documented. Prospective studies with intensive diagnostic efforts during the initial work-up have failed to identify any etiologic agent in more than one-half of patients hospitalized for CAP (46, 47). No currently available combination of clinical, radiologic, or laboratory characteristics reliably distinguishes patients who have viral, bacterial, or viral-bacterial coinfections, making it difficult to ascertain the need for antibacterial therapy in addition to antiviral therapy if such is available (47). In deciding whether to treat a patient with CAP who has a positive test result for a respiratory virus for a possible bacterial coinfection, two important risks must be weighed:

1. Risks of missed or delayed antibiotic treatment to patients with concomitant bacterial pneumonia (adverse outcomes and death) (42, 48–52)
2. Risks of antibiotic use to individual patients (side effects, disruption of microbiome, costs) and public health (antimicrobial resistance) (53)

Evidence synthesis. Our systematic review sought studies that enrolled patients with CAP and compared antibiotics versus no antibiotics after the identification of a viral respiratory pathogen by PCR. The literature search identified 3,895 articles, but, upon full-text review of 27 articles, none met our prespecified study selection criteria (lack of comparison or outcomes; *see* the online supplement for details). The search was then broadened to seek indirect evidence. Again, no studies met our prespecified study selection criteria. Therefore, no published studies were identified to inform the guideline committee's recommendations, and the guideline committee had to make clinical recommendations on the basis of noncomparative evidence and their nonsystematic clinical observations, which constitutes very low-quality evidence.

Committee's discussion. Given the lack of studies to inform the impact of antibiotics on outcomes for patients with CAP who have a positive test result for a respiratory virus, the committee addressed the question by combining epidemiologic evidence, pathophysiologic understanding, and clinical experience. We emphasize that the following recommendations are conditional and should be individualized on the basis of clinical judgment. Individual patient factors that strengthen or weaken each recommendation are provided in Table 1.

For outpatients, we recommend not offering empiric antibacterial therapy to every outpatient with CAP who has a positive test result for viral pathogen on the basis of *1*) the lack of epidemiologic studies that enrolled outpatients and evaluated the prevalence and outcomes of viral-bacterial codetection (54), and *2*) the committee's judgment that the low risk for an undesirable outcome if antibiotics are withheld or delayed means the potential benefits of early antibacterial therapy may not exceed the risks of harmful consequences of antibiotics to individual and public health. In contrast, we recommend administering empiric antibacterial therapy to adult outpatients who have comorbidities that might place them at risk for a serious outcome if antibiotics are withheld or delayed. There was disagreement among committee members regarding which comorbidities pose sufficient risk to warrant administering antibiotics to ambulatory patients with a detected viral pathogen. Factors discussed included those that increase the risk of either bacterial infection (decreased pulmonary clearance, impaired immunity) or poor outcomes from untreated bacterial coinfection (42). Table 5 depicts the results of the committee members' votes concerning comorbidities that support antibiotic therapy for outpatients with CAP who have a positive test result for a respiratory virus.

For inpatients hospitalized for CAP who have a positive test result for a respiratory virus, we suggest prescribing empiric antibiotics on the basis of *1*) ample medical literature documenting the coexistence of bacteria in patients who have pneumonia and have a positive test result for a respiratory virus, especially influenza virus and, to a lesser extent, respiratory syncytial and other respiratory viruses (47, 55, 56); and *2*) high risk of poor outcomes with viral-bacterial coinfection (43, 48), which likely increases if antibiotics are withheld or delayed in the event of bacterial infection (54). The committee recommendation for severe CAP was strong and unanimous despite very low quality of evidence, because insufficient antibiotic therapy can result in serious adverse outcomes or death in patients with severe CAP (1, 47, 49, 50, 57). A systematic review of epidemiologic studies evaluating the etiology of pneumonia among predominantly hospitalized patients reported that in studies in which viral PCR was performed, a respiratory virus was identified in 30–40% of patients, and bacteria were detected in 25–35% of these cases (58). The studies demonstrated that codetection of viral and bacterial pathogens in CAP caused by viruses other than SARS-CoV-2 occurred in about 25–30% of patients (47, 55, 59). A separate study that evaluated all patients hospitalized for CAP found to have a viral illness reported an 18–39% rate of bacterial detection (60). Prospective studies of CAP have shown the coincidence of viral and bacterial pathogens to vary from 3% to 19% (47, 59, 61). However, in these studies, there was widespread variation in sampling rates, and investigators failed to identify any etiologic agent in 37–62% of pneumonia cases. Using specialized techniques, a study limited to the small proportion of patients who could provide a high-quality purulent sputum sample at admission showed that, in addition to detection of usual bacterial pathogens, commensal bacteria, so-called normal respiratory flora, were present in an additional 8% of cases (58). The role of bacterial coinfection with commensal respiratory flora will not be recognized using currently available techniques.

The burden and consequences of bacterial coinfection may vary by viral pathogen. Recent studies of adults hospitalized for respiratory syncytial virus pneumonia show that 12–29% (62) have bacterial coinfection. Among patients hospitalized with SARS-CoV-2 virus during

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Table 5. Comorbidities that May Warrant Antibiotic Therapy for Outpatients with Community-acquired Pneumonia Who Have a Positive Test Result for a Respiratory Virus

Comorbidity (*See* Footnotes for Further Definitions and Examples)	Percentage of Committee Members Who Voted This Condition that May Warrant Antibiotics
Greater than 50% agreement	
Chronic pulmonary disease other than asthma	82
End-stage liver disease	71
End-stage renal disease	65
Cardiovascular disease	53
Alcoholism	53
Neoplastic disease	53
Less than 50% agreement	
Neurological disease	47
Chronic liver disease	35
Malnutrition	35
Current smoker	35
Corticosteroid therapy* (<20 mg daily or <4 wk)	30
Diabetes mellitus	29
Chronic kidney disease	24
HIV* (CD4, >200)	24
Asthma	21
Rheumatological diseases* (not receiving immunosuppressants)	18
Obesity (BMI, >30 kg/m^2)	12

Definition of abbreviation: BMI = body mass index.
Conditions are ranked by the percentage of committee members who would prescribe antibiotics for patients with each condition, in descending order. Chronic pulmonary diseases other than asthma are chronic obstructive pulmonary disease, bronchiectasis, or interstitial lung disease. End-stage liver disease includes ascites, variceal hemorrhage, hepatic encephalopathy, or renal impairment. End-stage renal disease includes glomerular filtration rate <15 ml/min lasting >3 months. Solid organ transplant recipient is defined as not receiving immunosuppressive antirejection medication. Cardiovascular disease includes congestive heart failure, coronary artery disease, or poorly controlled hypertension. Alcoholism is defined as recurrent or ongoing alcohol use despite inability to fulfill obligations or despite social or interpersonal problems exacerbated by alcohol use. Neoplastic disease is defined as not receiving immunosuppressive chemotherapy. Neurological disease includes Parkinson's disease, dementia, myasthenia gravis, or amyotrophic lateral sclerosis. Chronic liver disease is defined as abnormal liver function test results, coagulopathy, or other evidence of chronic liver damage lasting >3 months. Malnutrition is defined as weight loss, BMI <18.5 kg/m^2, reduced muscle mass, or reduced food intake or assimilation. Current smoker includes cigarettes and marijuana. Corticosteroid therapy was not at immunosuppressive doses such as a cumulative dose >600 mg of prednisone. Chronic kidney disease is defined as glomerular filtration rate 15–60 ml/min, albuminuria >30 mg/24 hours, or other markers of kidney damage lasting >3 months. HIV is defined as with CD4 >200 and no AIDS-defining illness. Rheumatological diseases include rheumatoid arthritis or systemic lupus erythematosus and not receiving immunosuppressive medication. Obesity is defined as BMI >30 kg/m^2.
*Patients with solid organ transplant receiving antirejection medications, corticosteroid therapy more than 20 mg/d for 4 weeks, HIV with CD4 count <200, or rheumatological diseases and receiving immunocompromising medication should be considered immunocompromised hosts to whom the community-acquired pneumonia guidelines do not apply. Refer to References 6 and 7 for guidance on diagnosis and management of these patients.

the pandemic, a systematic review of 24 studies indicated a low rate of bacterial coinfection (3.5%) (63), although a critical analysis has questioned the results of this review (64). A European cooperative study reported a 10% rate of bacterial detection in patients intubated with COVID-19, compared with 30% among patients with influenza (65). Whether this low rate of codetection in SARS-CoV-2 will remain in the future is uncertain.

Individual patient factors that strengthen or weaken the recommendation are provided in Table 1. The committee discussed whether features from the history or laboratory studies could reliably predict the presence of bacterial infection and thus the utility of antibiotics. However, we lack any clinical or laboratory parameters that individually or collectively reduce the probability of bacterial superinfection to a level that would allow safely withholding antibiotics. Although a high white blood cell count with the presence of band forms, an elevated procalcitonin concentration, or a delayed presentation could support a potential role for bacterial coinfection, the absence of these findings is not sufficiently reliable to exclude it for two reasons. First, the ability to predict microbiology on the basis of biomarkers is poor. For example, sensitivity and specificity of procalcitonin is, at best, approximately 75–80% (66, 67), and this performance may be worse in the setting of viral infection (68). Attempts to distinguish bacterial from viral causes of pneumonia on the basis of clinical criteria have also not been successful (47, 59). Second, even if these biomarkers were predictive of microbiology results, given that microbiology tests themselves are poor at identifying true bacterial infection in the lung, they are still insufficient to predict benefit or harm of antibiotics.

Because it is currently difficult to exclude the possibility of bacterial infection, the majority of the committee advised initiating antibacterial therapy in patients whose illness severity from pneumonia is sufficient to require hospitalization. However, the patient's presentation (Table 1), including comorbid conditions, clinical features, radiographic findings, virus identified, laboratory/microbiologic results,

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and clinical response, should be considered when reassessing the indication for continued antibiotics versus early discontinuation. We recommend that when empiric antibacterial therapy is initiated, clinicians should perform daily evaluations of clinical stability and review of microbiological results to inform deescalation or early discontinuation of antibacterial therapy. For specific recommendations regarding antimicrobial therapy including specific antibiotic regimens and antivirals, please refer to prior 2019 ATS/IDSA guidelines.

Recommendations.

1. For adult outpatients without comorbidities who have clinical and imaging evidence of CAP and who have a positive test result for a respiratory virus, we suggest not prescribing empiric antibiotics because of concern for bacterial-viral coinfection (conditional recommendation, very low-quality evidence). Remark: This is a conditional recommendation because the balance between benefit and harm of empiric antibiotics will vary on the basis of clinical context (*see* Table 1). Vote: 14 (93%) of 15 committee members voted in favor of NOT prescribing antibiotics.
2. For adult outpatients with comorbidities who have clinical and imaging evidence of CAP and who have a positive test result for a respiratory virus, we suggest prescribing empiric antibiotics because of concern for bacterial-viral coinfection (conditional recommendation, very low-quality evidence). Remark: This is a conditional recommendation because the balance between benefit and harm of empiric antibiotics will vary on the basis of clinical context (*see* Table 1). Vote: 11 (73%) of 15 committee members voted in favor of prescribing antibiotics.
3. For adult inpatients with clinical and imaging evidence of nonsevere CAP who have a positive test result for a respiratory virus, we suggest prescribing empiric antibiotics (conditional recommendation, very low-quality evidence). Remark: This is a conditional recommendation because the balance between benefit and harm of empiric antibiotics will vary on the basis of clinical context (Table 1). Vote: 12 (80%) of 15 committee members voted in favor of prescribing antibiotics.
4. For adult inpatients with clinical and imaging evidence of severe CAP who have a positive test result for a respiratory virus, we recommend prescribing empiric antibiotics (conditional recommendation, very low-quality evidence). Remark: Although the committee was unanimous in making this recommendation, this is a conditional recommendation because of the absence of comparative evidence. Vote: 15 (100%) of 15 committee members voted in favor of prescribing antibiotics.

What others are saying. Prior 2019 ATS/IDSA clinical practice guidelines recommended that standard antibacterial treatment be initially prescribed for adults with clinical and radiographic evidence of CAP who have a positive test result for influenza in both the inpatient and outpatient settings, based on multiple epidemiologic studies that reported high rates of detection of bacteria. The present update diverges from this recommendation for outpatients with CAP and influenza without comorbidities on the basis of the lack of epidemiologic evidence in outpatients, low risk of harm of withholding antibacterials in this population, and risks of antibiotic overuse to public health. The ATS guideline update addressing noninfluenza respiratory viral tests recommended against routine testing of viruses (3). Given the pandemic experience, the dynamic nature of viral epidemics, increasing availability of lower-cost tests, and potential for positive viral test results to change management, this recommendation may require future review. The decision when to obtain viral tests should be left to clinical judgment informed by both individual patient factors and local epidemiology. Guidelines for managing COVID-19 during the pandemic (4, 5) recommended that antibiotics not be administered unless there is evidence for bacterial coinfection on the basis of lower rates of bacterial detection observed during the pandemic. No guidelines have addressed whether to administer antibacterial therapy in patients with CAP who have a positive test result for other respiratory viruses, such as respiratory syncytial virus, because of the concern of bacterial coinfection (1, 69–71). Recent European Respiratory Society/European Society of Intensive Care Medicine/European Society of Clinical Microbiology and Infectious Diseases/Latin American Thoracic Association (ERS/ESICM/ESCMID/ALAT) guidelines for severe CAP recommend the use of molecular diagnostic PCR to detect both bacteria and virus when available, continue to recommend empiric antimicrobial for all patients, and highlight the need for studies that elucidate the safety of discontinuing antibiotics if bacterial test results are negative (72).

Research needs. There is an immediate need to improve the quality of evidence through comparative effectiveness research, including *1*) randomized controlled studies to determine which patients with CAP benefit from or are harmed by antibiotics when a virus is detected; *2*) studies that evaluate patients on the basis of the virus identified, illness severity, patient comorbidities, and for outcomes that impact patients beyond 30-day mortality (such as return to function and antibiotic-associated side effects); *3*) studies that compare the withholding of empiric antibiotics versus initiating and discontinuing them early (within the first 24–48 h of initiation) versus standard approaches; and *4*) studies of tailored approaches based on patient factors, including severity of illness presentation, patient- and virus-related risk of bacterial infection, and microbiological and biomarker information, including novel tests such as bacterial multiplex PCR, inflammatory markers, or host transcriptional signals (73, 74). Additional research is also needed to support appropriate use and interpretation of these tests, including which patient and environmental factors should be used to consider when to obtain viral testing.

Question 3: Should Adults with Community-acquired Pneumonia Who Reach Clinical Stability Be Treated with Less than 5 Days of Antibiotics?

Rationale. The optimal duration of antibiotic treatment in CAP is unknown. Because of concerns that pathogens may develop resistance if undertreated (75), prior CAP guidelines from the 1990s recommended antibiotic durations as long as 14 days, well beyond clinical stability (76, 77). However, as our model of lung infection advances, the goals of antibiotics may no longer be to completely eradicate causative pathogens (78) but rather to reduce bacterial load with as little disruption to the microbiome as possible (79). Harms from longer antibiotic durations are increasingly observed, including side effects (80, 81), *Clostridioides difficile* infection (82, 83), acute

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kidney injury (83), disruption of normal flora (84), and emergence of antibacterial resistance (85, 86). Over the past two decades, several studies have demonstrated noninferior clinical outcomes with shorter durations of antibiotic therapy compared with longer durations (87–91). ATS/IDSA CAP guidelines in both 2007 and 2019 recommended a duration of antibiotic therapy no more than 5 days if the patient reaches clinical stability. Since these recommendations, additional clinical trials suggested that durations shorter than 5 days could be adequate for selected patients reaching clinical stability.

Evidence synthesis. The initial evidence synthesis included 13 studies of immunocompetent patients with clinical and imaging evidence of CAP that evaluated any antibiotic as long as it involved less than 5 days of treatment. This was changed to include only studies evaluating less than 5 days of effective duration so that studies of azithromycin were included only if it was administered for less than 3 days because of the pharmacokinetics of azithromycin (1 d of high-dose 2-g azithromycin microspheres are effectively 4 d in duration, and 3 d of 500-mg or 1-g azithromycin are effectively 5 d or slightly longer in antibiotic duration) (92, 93). Several studies in which azithromycin was administered for 3 days were thus removed. Our systematic review identified four relevant randomized controlled trials that compared $<$5 effective days' duration of antimicrobial therapy with $\geqslant$5 days' duration (87, 89, 94, 95). Two of the trials evaluated azithromycin in outpatients: D'Ignacio and colleagues compared 1 day of 2-g extended-release azithromycin with 7 days of 500-mg levofloxacin, and Drehobl and colleagues compared 1 day of 2-g extended-release azithromycin with 7 days of 1-g extended-release clarithromycin (94, 95). These were considered an assessment of effectively 3 days' duration of antimicrobial therapy, given the pharmacokinetics of azithromycin; four studies evaluating 3 days of azithromycin were not included. The other two trials used β-lactams and enrolled hospitalized patients. In immunocompetent nonpregnant inpatients with mild or moderate pneumonia admitted to hospital wards who had clinical improvement after a 3-day course of high-dose intravenous amoxicillin, Moussaoui and colleagues compared placebo with 5 additional days of 750-mg amoxicillin by mouth three times daily. Among immunocompetent hospitalized patients without a history of respiratory insufficiency or severe or complicated pneumonia who reached clinical stability after a 3-day course of a β-lactam antibiotic, Dinh and colleagues compared placebo with 5 additional days of 1-g/125-mg oral amoxicillin-clavulanate (87, 89) (Table E4 and Table E5). The studies used different definitions of clinical cure and had variable follow-up time periods, although the follow-up periods could be classified as either 1–2 weeks or 3–4 weeks after treatment initiation.

The guideline committee *a priori* defined three outcomes as "critical," which included mortality, treatment success/failure, and CAP complications. Out of these outcomes, only mortality and treatment success (defined by studies as clinical cure) could be estimated from the included studies. The committee also *a priori* defined five outcomes as "important," including duration of hospitalization, antibiotic-free days, patient experience, cost, and antibiotic resistance. Out of these outcomes, only one study evaluated duration of hospitalization.

The data were aggregated by meta-analysis for each outcome (Figure E5). Mortality was evaluated in only one study (Dinh and colleagues), which showed no statistically significant difference when fewer than 5 days of antibiotics were compared with 5 or more days (2.0% vs. 1.3%; risk ratio, 1.49; 95% CI, 0.25 to 8.79). One death occurred among patients treated with fewer than 5 days of antibiotics; the patient had bacteremia caused by *Staphylococcus aureus.* One death occurred among patients treated with more than 5 days of antibiotics; the patient had recurrent pneumonia. The clinical cure rate 1–2 weeks after treatment was similar among patients who received less than 5 days of antibiotics versus those who received 5 or more days (85.6% vs. 87.6%; risk ratio, 0.98; 95% CI, 0.91 to 1.05) (Figure E5 and Table E6.1).

Subgroup analyses for clinical cure rate 1–2 weeks after treatment were based on the setting and antibiotic. For the subgroup of outpatients treated with azithromycin, the clinical cure rate 1–2 weeks after treatment was similar among patients treated with less than 5 days of antibiotics compared with 5 or more days of antibiotics (87.4% vs. 91.9%; risk ratio, 0.96; 95% CI, 0.91 to 1.01) (Figure E5 and Table E6.2). Likewise, for the subgroup of inpatients treated with β-lactams, the clinical cure rate 1–2 weeks after treatment was similar among patients treated with less than 5 days of antibiotics versus those treated for 5 or more days (81.9% vs. 75.7%; risk ratio, 1.06; 95% CI, 0.90 to 1.24) (Figure E5 and Table E6.3).

Clinical cure rate 3–4 weeks after treatment was similar among patients who received less than 5 days of antibiotics versus those who received 5 or more days (81.0% vs. 82.5%; risk ratio, 0.99; 95% CI, 0.92 to 1.07) (Figure E5 and Table E6.1). For the studies evaluating azithromycin in outpatients, the clinical cure rate 3–4 weeks after treatment was similar among patients treated with less than 5 days of antibiotics versus those treated with 5 or more days (82.1% vs. 84.1%; risk ratio, 0.98; 95% CI, 0.84 to 1.13) (Figure E5 and Table E6.2). For the studies evaluating β-lactams among inpatients, the clinical cure rate 3–4 weeks after treatment was also similar among patients treated with less than 5 days of antibiotics versus those treated with 5 or more days (78.7% vs. 79.2%; risk ratio, 1.01; 95% CI, 0.92 to 1.11) (Figure E5 and Table E6.3).

Hospital length of stay was not impacted by whether subjects were treated with less than 5 days or with 5 or more days of antibiotics (mean, 6 ± 3.7 d vs. 6.3 ± 3.7 d; mean difference, -0.35 d; 95% CI, -1.17 to 0.47 d) (Figure E5 and Table E6.3). Overall, the committee's certainty in the accuracy of the estimated effects (the quality of evidence) was low (Table E6).

Committee's discussion. Our recommendation for antibiotic duration in adults with CAP who reach clinical stability varies on the basis of CAP severity and treatment setting. Table 6 defines clinical stability according to the study definitions.

For immunocompetent adult outpatients and inpatients with nonsevere CAP who reach clinical stability, we suggest treating with $<$5 days' effective duration of antibiotics (minimum of 3 d) rather than $\geqslant$5 days of antibiotics because of the four recent trials that suggested similar clinical outcomes in these groups. The pharmacokinetics of the antibiotic and the patient's renal and hepatic function must be considered to establish the number of days of treatment that are equivalent to the suggested therapeutic duration (the effective number of days), particularly for macrolides (which have a half-life of 3 d) and for patients with renal insufficiency.

We recognize that the existing studies *1*) established noninferiority but not clinical benefit of shorter durations in a select group of patients, excluding many patients with comorbidities; *2*) did not evaluate important

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Table 6. Clinical Stability Definitions*

Temperature	≤37.8°C
Heart rate	<100 beats per minute*
Respiratory rate	<24 breaths per minute*
Arterial oxygen saturation or partial pressure	Sp_{O_2} ≥90% or Pa_{O_2} ≥60 mm Hg on room air* or baseline oxygen requirement†
Systolic blood pressure	≥90 mm Hg
Mental status	Normal

Definition of abbreviation: Sp_{O_2} = oxygen saturation as measured by pulse oximetry.
The duration of antibiotics should be determined on the basis of daily assessment of clinical responses.
*All criteria needed to be met to be considered "stable" in the Dinh and colleagues study (89). Prior 2007 guidelines and the Uranga and colleagues study (88) required the patient to be afebrile plus having no more than one sign of instability and used a heart rate ≤100 beats per minute and respiratory rate ≤24 breaths per minute. For the el Moussaoui and colleagues study, eligibility for 3-day duration was determined by improvement of 2 or more points on a respiratory symptom scale, temperature <38°C, and ability to perform oral intake.
†Neither the Dinh and colleagues nor the el Moussaoui and colleagues study included patients with chronic respiratory insufficiency. Thus, this factor weakens this recommendation (*see* Table 1).

outcomes such as CAP-related complications or return to baseline function; and *3*) examined antibiotic selection and doses that are not considered appropriate treatment by the IDSA/ATS (azithromycin and clarithromycin are not considered adequate treatment for outpatients because of the high rate of macrolide-resistant *Streptococcus pneumoniae* in the United States; combination therapy of β-lactam plus macrolide or fluoroquinolone is strongly recommended for inpatients; and fluoroquinolone dosing for CAP is 750-mg levofloxacin or 400-mg moxifloxacin).

For outpatients, many meet clinical stability criteria upon presentation, but individual patient factors (listed in Table 1) should be considered for appropriateness, and all patients should be monitored for clinical recovery or recurrent infection. Assessing the safety of discontinuing antibiotics on Day 3 requires close follow-up, which may be difficult in some settings and patients. If prescribing short courses of antibiotics, clinicians and patients should develop an optimal plan based on individual patient preferences, discuss signs and symptoms of recovery or recurrence of infection (elevated temperature or heart rate, shortness of breath, altered mental status), and establish communication lines and contingency plans.

For inpatients with nonsevere CAP, this recommendation should be applied only to those patients who do not have additional contraindications to short courses of antibiotics and who reach clinical stability, including resolution of new oxygen needs. Table 1 lists additional patient factors to consider, such as patient comorbidities and results of inflammatory markers. Antibiotic courses should not be implemented as a set duration for all patients determined at presentation, because many patients have contraindications to shorter durations, and time to clinical stability is difficult to predict on presentation. The duration of antibiotics should be determined day by day on the basis of clinical responses. A sizable proportion (over 50%) of hospitalized patients with nonsevere CAP would not be eligible for short courses (96–99). Patients discharged home should also establish clear follow-up plans for symptoms of recurrence.

Adults with severe CAP were not evaluated in the trials we reviewed. We thus maintain our prior strong recommendation of 5 days or greater because of these patients' higher risk of disseminated infection, necrotizing or resistant organisms, and higher risk and consequences of treatment failure.

Regardless of illness severity, patients with contraindications to shorter courses, including severe chronic lung disease such as bronchiectasis, evidence of necrotizing pneumonia such as lung abscesses or empyema, or confirmed infection with a necrotizing or resistant organism such as *Staphylococcus aureus* or *Pseudomonas aeruginosa* require tailored antimicrobials according to guidance specific to these complications. In patients with low certainty of a CAP diagnosis who have an alternative diagnosis that better explains their illness, antibiotics should be discontinued. This is not a short course for pneumonia but an individualized treatment based on refined diagnosis.

Recommendations.

1. For adult outpatients with CAP who reach clinical stability, we suggest less than 5 days of antibiotics (minimum of 3-d duration) rather than 5 or more days of antibiotics (conditional recommendation, low-quality evidence). Remark: This is a conditional recommendation that requires individualization. *See* Table 1 for factors that weaken this recommendation. Vote: 15 (94%) of 16 committee members voted in favor of less than 5 days of antibiotics.
2. For adult inpatients with nonsevere CAP who reach clinical stability, we suggest less than 5 days of antibiotics (minimum of 3-d duration) rather than 5 or more days of antibiotics (conditional recommendation, low-quality evidence). Remark: This is a conditional recommendation that requires individualization. *See* Table 1 for factors that weaken this recommendation. Vote: 11 (69%) of 16 committee members voted in favor of less than 5 days of antibiotics.
3. For adult inpatients with severe CAP who reach clinical stability, we suggest 5 or more days of antibiotics rather than less than 5 days of antibiotics (strong recommendation, low-quality evidence). Remark: This recommendation is strong despite the low quality of evidence because robust evidence indicates that insufficient antibiotic therapy can result in serious adverse outcomes or death in patients with severe CAP. Note: 15 (94%) of 16 committee members voted for 5 days or more of antibiotics.

What others are saying. British Thoracic Society guidelines (2009) and National Institute for Health and Care Excellence guidelines (2015) for the management of CAP recommended a 5-day course of a single antibiotic for patients with low-severity CAP and 7–10 days' duration

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for patients with moderate or severe CAP (100, 101). However, it should be noted that these society guidelines do not endorse the same empiric strategy of antibiotics recommended by IDSA/ATS. ERS and ESCMID guidelines for the management of lower respiratory tract infections (2011) recommended antibiotics for 7 days among inpatients with nonsevere CAP (71). Consensus guidelines for the management of severe CAP issued by ERS/ESICM/ESCMID/ALAT (102) (2023) conditionally recommend that procalcitonin may be used to reduce the duration of antibiotic treatment in patients with severe CAP when the duration of antibiotic therapy was over 7 days. In the case of durations less than 5 days, the utility of inflammatory markers has not been addressed.

Research needs. Our recommendations are conditional based on low quality of evidence, and the optimal duration of therapy for patients with CAP once they reach clinical stability is still unknown. Research needed to better inform this recommendation includes clinical trials that evaluate *1*) first-line therapies; *2*) outcomes that are important to patients, such as development of complications (whether from the infection or the antibiotic treatment), long-term outcomes, antibiotic effects, length of hospitalizations, and return to function; and *3*) tailored strategies based on pathogen identification, illness severity (nonsevere vs. severe CAP), clinical response, and serial inflammatory markers.

Question 4: Should Adults Who Are Hospitalized with Community-acquired Pneumonia Be Treated with Corticosteroids?

Rationale. The host immune response to infection is an increasingly recognized factor influencing mortality and morbidity in patients with CAP. Treatments that target immunomodulation such as corticosteroids have historically had mixed results. The 2019 ATS/IDSA guideline for the management of adults with CAP previously reviewed the question whether corticosteroids should be included as part of the treatment regimen for adults with CAP. The guideline committee recommended against routine use of corticosteroids in adults with nonsevere CAP (strong recommendation, high quality of evidence) and suggested against their routine use in adults with severe CAP (conditional recommendation, moderate quality of evidence). These recommendations were based on the review of four meta-analyses of published trials, two of which reported a mortality benefit in patients with severe CAP (103, 104) and two of which did not find a benefit (105, 106). Since the publication of those guidelines, several additional trials have been published evaluating the effect of corticosteroids on mortality and other CAP outcomes, including one trial that demonstrated a significant mortality benefit when steroids were prescribed in severe CAP (107). In addition, the 2021 publication of the RECOVERY (Randomized Evaluation of COVID-19 Therapy) trial demonstrated a strong benefit of corticosteroids in patients with moderate to severe COVID-19 during the pandemic, particularly in patients who required oxygen by high-flow nasal cannula or invasive mechanical ventilation (108). These new studies and experiences add weight to a pathophysiologic mechanism of benefit of immunomodulation for select patients with pneumonia, led others to update their recommendations (102, 109), and support the need to reassess the evidence regarding use of corticosteroids in adults with CAP.

Evidence synthesis. Our literature search identified 16 relevant studies (107, 110–124). One relevant study was excluded because it was retrospective (111), leaving 15 randomized controlled trials for analysis (107, 110, 112–124). All trials enrolled inpatients but used varying definitions of CAP. Six trials evaluated hydrocortisone therapy (107, 112, 115, 119, 120, 123), and the remaining trials examined methylprednisolone (three trials) (113, 116, 122), dexamethasone (three trials) (114, 117, 124), and prednisone/prednisolone (three trials) (110, 118, 121). The duration of corticosteroids varied among trials but included 7 days (five trials) (110, 112, 119–121), 5 days or fewer (seven trials) (114, 115, 117, 118, 122–124), and longer durations (three trials) (107, 113, 116) (Table E7).

The guideline committee *a priori* defined four outcomes as "critical": mortality, treatment/clinical failure, clinical stability, and adverse drug events. The committee also *a priori* defined four outcomes as "important": symptoms, disability or return to independence/function, length of stay, and antibiotic days. Given a lack of consistent measurement of symptomatic improvement, return to function/independence, or disability across the selected trials, these outcomes were not evaluated.

When the data were aggregated by meta-analysis, corticosteroids decreased mortality (6.1% vs. 9.1%; risk ratio, 0.68; 95% CI, 0.53 to 0.86), which means that if applied to a population similar to that enrolled in the trials, it is estimated that one death would be prevented for every 34 (range, 23–78) patients who received corticosteroids (Figure E8 and Table E8.1). In patients with nonsevere CAP (117, 124), the decrease in mortality was not statistically significant (4.4% vs. 6.7%; risk ratio, 0.88; 95% CI, 0.55 to 1.41) (Figure E8 and Table E8.3). When the meta-analysis was restricted to patients with severe CAP (107, 112, 115, 116, 120, 122), the decrease in mortality was significant (9.8% vs. 15.1%; risk ratio, 0.62; 95% CI, 0.41 to 0.94), meaning that one death could be prevented for every 17 (95% CI, 11–110) patients with severe CAP who receive corticosteroids (Figure E8 and Table E8.2).

Corticosteroids also decreased the length of stay (mean difference, −1.53 d; 95% CI, −2.14 to −0.91 d) (Figure E8 and Table E8.1) (110, 112, 113–119, 121, 122, 124). The decrease in the length of stay was not statistically significant in patients with nonsevere CAP (mean difference, −0.52 d; 95% CI, −1.33 to 0.28) (Figure E8 and Table E8.3) but was significant for patients with severe CAP (mean difference, −1.06 d; 95% CI, −2.01 to −0.12) (Figure E8 and Table E8.2).

There was no significant effect on adverse events (risk ratio, 1.2; 95% CI, 0.89–1.63) (Figure E8 and Table E8.1), including the subgroups of patients with nonsevere CAP (risk ratio, 1.37; 95% CI, 0.73 to 2.43) and severe CAP (risk ratio, 1.12; 95% CI, 0.69 to 1.82) (Figure E8 and Table E8.2). Corticosteroid therapy did not demonstrate an effect on treatment failure (risk ratio, 0.83; 95% CI, 0.25 to 2.80) or time to clinical stability (mean difference, −0.45 d; 95% CI, −1.77 to 0.86 d). There was no effect on antibiotic duration (mean difference, −2.01 d; 95% CI, −4.46 to 0.45 d), including the subgroup of patients with nonsevere CAP (mean difference, −0.99; 95% CI, −3.93 to 1.96) (Table E8.1). Overall, the committee's certainty in the accuracy of the estimated effects (the quality of evidence) was low for both severe and nonsevere CAP because of inconsistency of results (Table E8).

Committee's discussion. The committee evaluated the evidence for corticosteroids in inpatient adults with nonsevere CAP and

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severe CAP (as defined by ATS criteria) separately. For adult inpatients with nonsevere CAP, the committee judged that because no significant difference was observed in mortality or other critical outcomes in pooled analyses, the undesirable effects of corticosteroids outweighed desirable effects. However, this recommendation does not obviate the need to administer corticosteroids for other indications in this group, such as chronic obstructive pulmonary disease or asthma exacerbations or suspicion for pneumocystis pneumonia.

In severe CAP, the committee judged that the desirable effects of steroids on critical outcomes, particularly mortality, outweighed the undesirable effects, predominantly hyperglycemia, and that the intervention is feasible and likely to be acceptable to most patients when considering patient preferences and values. The recommendation in favor of corticosteroids is conditional because our confidence in the quality of the evidence was low, in large part because of inconsistency of results across studies. Notably, the study by Dequin and colleagues (107) found a significant reduction in mortality, whereas the study by Meduri and colleagues (116) did not. Important differences in the Dequin and colleagues study that may have contributed to the positive findings include *1*) earlier exposure to corticosteroids from the diagnosis of severe CAP, *2*) criteria for severe CAP that focused on respiratory failure (and did not include patients with septic shock), *3*) exclusion of patients with influenza, and *4*) inclusion of more women. Although the committee endorses the ATS/IDSA definition of severe CAP as including need for either mechanical ventilation or vasopressor support (major criteria) or three or more minor criteria (1), we recognize heterogeneity within this group and note that the aggregate meta-analysis approach is limited in its ability to identify specific subgroups of patients who benefit most from corticosteroids. For example, an individual patient data meta-analysis of eight clinical trials identified elevated C-reactive protein as a predictor of corticosteroid benefit (125). Since the completion of our evidence review, the REMAP-CAP platform trial (A Randomized, Embedded, Multifactorial, Adaptive Platform Trial for Community-Acquired Pneumonia) reported results for fixed-dose hydrocortisone, which demonstrated no benefit regarding short-term mortality, although the shock-dependent arm and both dexamethasone arms are still ongoing (126). In addition, a preplanned subgroup analysis of the APROCCHSS (Activated Protein C and Corticosteroids for Human Septic Shock) trial evaluating corticosteroids in septic shock was also published after our evidence review, finding a significant benefit of hydrocortisone with fludrocortisone in those with septic shock caused by CAP but not of non-CAP causes (127), in contrast to the earlier ADRENAL (Adjunctive Corticosteroid Treatment in Critically Ill Patients with Septic Shock) study published in 2018 (128). A subsequent meta-analysis that included these trials reported a continued overall favorable effect of corticosteroids (129). The inconsistency of results further highlights the uncertainty of benefit for many patients and the need to individualize the decision to treat with corticosteroids. We eagerly await additional evidence surrounding different patient phenotypes to improve precision with CAP treatment and anticipate that this recommendation will be further refined on the basis of new evidence in the future. *See* Table 1 for additional patient characteristics that would strengthen or weaken this recommendation, including clinically available markers of inflammation that that may be useful to predict benefit versus harm.

Although the exact mechanism of the benefit of corticosteroids in these patients is unclear, the timing (early administration) and pattern of inflammatory response (elevated inflammatory markers, particularly C-reactive protein) may be important factors to consider when deciding which patients are most likely to benefit (125). This suggestion should not be applied to patients with CAP and influenza, because observational data suggest potential harm (130), and there is a lack of prospective, randomized data in this population because they were excluded from most of the trials. Currently available evidence precludes a recommendation on the type of corticosteroid and duration of exposure, although the trial with the most compelling results assigned patients to hydrocortisone 200 mg continuous intravenous infusion daily for either 4 or 7 days as determined by clinical improvement followed by tapering for a total of 8 or 14 days or discontinuation of corticosteroids at ICU discharge among those patients with rapid clinical improvement (107).

Recommendations.

1. For adult inpatients with nonsevere CAP, we recommend not administering systemic corticosteroids (strong recommendation, low quality of evidence). Remark: This recommendation is strong because, although the overall quality of evidence is low, the intent is to avoid harmful side effects such as hyperglycemia, for which there is robust evidence. Vote: 16 (100%) of 16 committee members voted in favor of not administering systemic corticosteroids.
2. For adult inpatients with severe CAP, we suggest administering systemic corticosteroids (conditional recommendation, low quality of evidence). Remark: This recommendation excludes patients with severe CAP caused by influenza pneumonia. Vote: 15 (94%) of 16 committee members voted for administering systemic corticosteroids.

What others are saying. The ERS/ESICM/ESCMID/ALAT guidelines published in 2023 suggest using systemic corticosteroids in severe CAP only if shock is present (conditional recommendation, very low quality of evidence) (102). This guideline did not include the study by Dequin and colleagues (107). The Society of Critical Care Medicine focused guideline update on corticosteroids recommends administering corticosteroids to adult patients hospitalized with severe bacterial CAP (strong recommendation, moderate certainty; "bacterial CAP" defined as probable or suspected bacteria) and makes no recommendation for administering corticosteroids for adult patients hospitalized with nonsevere CAP (109). The Surviving Sepsis Campaign recommends use of corticosteroids in patients with septic shock refractory to adequate fluid resuscitation and vasopressor support (131), as well as the recent update on management of adult patients with acute respiratory distress syndrome suggesting using corticosteroids in these patients (132). The NIH COVID-19 treatment guidelines (5) also recommended corticosteroids (specifically dexamethasone) for the treatment of COVID-19 pneumonia in hospitalized patients who required supplemental oxygen, particularly high-flow nasal cannula, noninvasive ventilation, or invasive mechanical ventilation, although the certainty of benefit in patients with CAP caused by SARS-CoV-2 outside of the pandemic may be lower. In addition, clinicians should use corticosteroids when

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deemed clinically appropriate for comorbid conditions, such as chronic obstructive pulmonary disease, asthma, and autoimmune diseases, in which corticosteroids are supported as a component of treatment. Multiple systematic reviews have also been published that, like the systematic review that informed our recommendations, reported benefits from systemic corticosteroids in patients with severe CAP (133–135).

Research needs. Three types of research are needed to help strengthen the evidence base informing the use of corticosteroids in CAP: trials that evaluate *1*) which patient features are associated with benefit, including those adequately designed to evaluate patient subgroups or tailored strategies based on sex, severity of respiratory failure/acute respiratory distress syndrome, inflammatory biomarkers, pathogen identification, or other key features subgroups yet to be identified; *2*) optimal dose, duration, type, and timing of corticosteroid treatment relative to onset of CAP; and *3*) outcomes in addition to mortality, such as time to clinical stability, treatment failure, impact on nonpulmonary complications of CAP (e.g., cardiovascular events), and long-term outcomes (e.g., symptom burden, functional status, and health-related quality of life). Patients with influenza should be included in this research, because data supporting their exclusion are limited to very low-quality observational studies in this population.

Patient Input

For all CAP recommendations, high-quality communication with patients should cover *1*) the rationale for the clinical recommendation; *2*) the degree of certainty for the recommendation; *3*) the advantages and disadvantages of treatment options, including side effects, cost, and convenience; *4*) what to expect over the course of treatment, including clear access to follow-up and contingency plans; and *5*) a pathway for communication and follow-up. Recommendations with less certainty should be accompanied by greater engagement with patients about their preferences and values.

When deciding whether to pursue LUS or chest radiography for diagnosis, discussions with patients should include convenience, accuracy, cost, and radiation exposure, as well as clinician expertise and the facility's ability to conduct, interpret, and document US results. The potential for each test to identify incidental findings should be considered. When weighing the decision regarding antibiotic use when a viral test result is positive, patients should be informed that antibiotics do not treat viruses and may have side effects but that bacteria and viruses can coexist. Less aggressive antibiotic therapy (no treatment or short courses) should be coupled with more aggressive monitoring and follow-up, including a clear and feasible contingency plan if a patient's condition does not improve or a patient experiences side effects. Clear definitions of clinical stability and antibiotic side effects should be communicated to patients. When considering corticosteroids, clinicians should provide realistic expectations, including uncertainty about treatment effects for any individual patient and risks of short-term versus chronic use.

Clinicians should use common language and patient information documents to explain medical concepts and adopt a tailored approach to communication based on the patient's severity of illness, ability or preference to engage in communication or shared decision making, and degree of certainty of the benefit of recommendations. Documents that provide patient-friendly explanations of pneumonia should be used to support communication and are available through the ATS (136, 137).

Conclusions

This document addresses four practice areas pertaining to the management of patients with CAP. These areas were selected by the committee because of their clinical relevance and the potential influence of recent literature on the existing standard of care.

For the purpose of diagnosing pneumonia, the use of LUS is regarded as equivalent to chest radiography, provided there is sufficient clinical expertise and infrastructure available. Concerning the use of antibacterial therapy for patients diagnosed with a respiratory virus, the suggestion is to withhold antibacterial therapy only in outpatients who do not have coexisting medical conditions that put them at risk of severe outcomes. Addressing the optimal duration of antibiotic therapy, $<$5 days of treatment is regarded as acceptable (minimum of 3-d duration), except in case of severe CAP or pneumonia caused by necrotizing or resistant organisms, such as *S. aureus* or *P. aeruginosa*. Last, the use of systemic corticosteroids is endorsed solely for a subgroup of patients experiencing severe CAP without influenza virus infection.

However, practitioners must acknowledge that most recommendations presented in this document are based on low-quality evidence or have low or very low certainty of effects. This implies that new studies are likely to have an important influence on the estimate of the effect and that the true effect might be substantially different from the estimated effect. We encourage research efforts to improve the evidence surrounding pneumonia care, particularly by conducting studies that evaluate patient-oriented outcomes in the areas of diagnosis, individualize antimicrobial treatments and host-directed therapies, and also evaluate the relationships between CAP management of individual patients and public health outcomes such as antimicrobial resistance and infection transmission.

Given the potential impact of future research on our current recommendations, it is crucial for physicians to thoroughly assess patients when implementing a clinical approach on the basis of these recommendations and to individualize their management according to patients' risks and clinical responses. We encourage a nuanced clinical approach to pneumonia care that acknowledges the complexity of lung disease and uncertainty in the evidence base. ■

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Online Supplement

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… on behalf of the American Thoracic Society Assembly on Pulmonary Infections and Tuberculosis.

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METHODS

Panel Composition

The project was proposed by one of the co-chairs (BJ) through an application to the American Thoracic Society (ATS), which subsequently invited the Infectious Diseases Society of America (IDSA) to collaborate. The project began January 1, 2022. Cochairs BJ and JR proposed panelists based upon their expertise in the diagnosis and management of community-acquired pneumonia (CAP) and KCW assembled a methodology team from the ATS' Guideline Methodology Training Program (EO, BB, SL, BE). The committee was diverse with respect to gender, specialties (pulmonology, infectious disease, internal medicine, critical care, hospital medicine, emergency medicine, and evidence synthesis), level of seniority, and geographical locations. The appointed representatives from ATS and IDSA were approved by the leadership of those societies. All panelists disclosed their conflicts of interest, which were vetted and managed according to the policies and procedures of the ATS and IDSA.

Questions

The co-chairs drafted key questions pertaining to treatment interventions in a PICO (Population, Intervention, Comparator, and Outcome) format. The questions were discussed, revised, and finally approved by the full committee at a virtual meeting Fall 2022. Four PICO questions were agreed upon. For each PICO question, critical and important outcomes were predetermined. An overview document was created to clarify inclusion and exclusion criteria, participants, and *a priori* subgroup analyses.

Literature search

The published literature was searched by a health librarian (MH) as well as reviewed by the lead methodologist (EO) in a number of databases, including Medline/PubMed, Excerpta Medica Database (EMBASE), and Cochrane Database of Systematic Reviews. Searching was conducted Winter and Spring 2023. The methodology team reviewed all publications retrieved from the literature searches, initially screening based on title and/or abstract and then reviewing the full text of potentially relevant publications. Bibliographies of selected studies, relevant systematic reviews, and articles suggested by committee members were also reviewed. All screened article meta-fields were input into Rayyan.AI, which was used to document and track included and excluded articles for full-text review. Randomized trials that compared performing the treatment of interest to not performing the treatment were sought first. If randomized trials were not identified, non-randomized studies that compared performing a treatment to not performing the treatment were sought. If such studies were not found, non-randomized studies without a control group were sought. If no direct evidence was found, indirect evidence (e.g. population, intervention) was sought based on initial expert discussion. For one of the PICO questions, this resulted in a shift to diagnostic interventions, with inclusion of accuracy studies that determined sensitivity and specificity of the diagnostic test.

Evidence synthesis

Findings from selected publications were extracted into an Excel spreadsheet created specifically for the project. When data were amenable to weighted pooling (i.e., meta-analysis), a random effects model was implemented in the Cochrane Collaboration Review Manager (RevMan), version 5.4. For controlled studies, relative risk (RR) was used to report dichotomous outcomes and the mean difference (MD) was used to report continuous outcomes. The accompanying 95% confidence interval (CI) was determined.

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Statistical heterogeneity was measured using the I^2 test; an I^2 ≥75%, 50-75%, and 25-50% was considered severe, moderate, and mild, respectively. Whenever heterogeneity was encountered, sensitivity analyses were performed to identify contributing studies, reasons for the heterogeneity sought, and subgroups analyzed. If no cause was found, we eliminated outliers and the estimates before and after elimination of outliers were both presented to the committee to inform their discussion and judgements. Results are provided in the evidence tables. For diagnostic comparisons, a summary receiver operator curve was constructed. The area under the curve was calculated and a bivariate model was used to find a single best estimate of sensitivity and specificity.

The Grading, Recommendations, Assessment, Development, and Evaluation (GRADE) approach was used to assess certainty in the estimated effects (i.e., the quality of evidence) for each intervention on each outcome of interest. The methodology team created evidence profiles, which categorized the overall certainty in the evidence into one of four levels: high, moderate, low, or very low. Each level represents the certainty in the accuracy of the estimated effects for a specific intervention. The full guideline panel reviewed the evidence profiles and provided input and feedback.

Recommendations

The methodology team distributed the completed evidence syntheses to the guideline committee by email two weeks prior to the face-to-face meeting at the ATS conference in Washington DC, May 2023. The methodology team presented the evidence syntheses at the meeting, which were then discussed by the committee and recommendations were formulated. Decisions about whether to recommend for or against an intervention were based on the balance of desirable consequences (benefits) and undesirable consequences (burdens, adverse effects, and costs), quality of evidence, feasibility, and acceptability to patients (i.e., patient values and preferences). Guideline committee members were encouraged to consider their non-systematic clinical observations (i.e., clinical experience) when the quality of empirical evidence was very low.

To facilitate consensus, each recommendation was voted on using the Convergence of Opinion on Recommendations and Evidence (CORE) approach, a modified Delphi process. Voting percentages were calculated and rounded to the nearest multiple of five. It was decided a priori that 1) 80% committee participation was necessary, 2) 70% agreement was necessary to make a recommendation, 3) the strength of the recommendation would be determined by the majority among those in agreement, and 4) only those who were present for the evidence presentation could vote on the recommendation. The methodology team and patient representatives were not voting members of guideline committee.

Evidence to Data (EtD) tables were constructed for each PICO question summarizing recommendations and providing an overview of the process.

Implications of the strength of recommendations

The strength of recommendations can be conceptualized in several ways. First, “we recommend” conveys that the recommended course of action is the appropriate in >95% of patients, whereas a “we suggest” conveys that the recommended course of action is appropriate in >50% of patients but may not be appropriate in a sizeable minority. Second, “we recommend” conveys “just do it”, whereas ”we suggest” conveys “slow down, think about it, discuss it”. Third, a ”we recommend” conveys that

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criticism may be warranted if the recommended course of action is not followed, whereas ”we suggest” conveys that a decision to not follow the recommended course of action may be a matter of style or equipoise. Finally, ”we recommend” is often the basis of a performance measure, whereas ”we suggest” seldom make reasonable performance measures.

Manuscript preparation

The introduction and outline were written by the co-chairs (BJ, JR). Guideline committee members were assigned to subcommittees to create sections of the manuscript. The sections were collated and edited into a single manuscript by BJ and JR. All members of the guideline committee reviewed the manuscript; comments were addressed by the co-chairs and then incorporated into the revised manuscript. The manuscript was redistributed to the full committee for further review. The final product was the result of collective work from the co-chairs, committee members, methodologists, and health librarian. Once the manuscript was approved by the full guideline committee, it was submitted for external peer review.

Peer review and approval

Peer review was overseen by the ATS Associate Documents Editor. The guideline was reviewed independently by each co-sponsoring society. This included anonymous peer review by both content experts and guideline methodology experts. Following multiple cycles of review and revision, the guideline was reviewed and approved by the ATS Board of Directors. The IDSA chose to withdraw rather than approve the final version of the guideline.

Updating

The guideline will be reviewed by the ATS’ Pulmonary Infections and Tuberculosis Assembly within five years. If one or more questions are deemed in need of an update, or related new questions need answered, a new task force may be approved to develop an updated guideline.

Funding

Funding was provided by both the American Thoracic Society.

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PICO question #1: Lung ultrasound versus chest x-ray to diagnose CAP

Population: Adults with suspected community-acquired pneumonia

Intervention: Ultrasound, in addition to clinical judgment

Comparator: Chest x-ray, along with clinical judgment

Outcomes:

Critical

Time to appropriate diagnosis, treatment, and disposition (including emergency department length of stay)

Accuracy/Performance characteristics (sensitivity, specificity,)

Repeat visit to emergency department, clinic, or hospital/re-admission

Important

Provider experience (e.g. clinician confidence in decision-making, usability, etc.)

Us of advanced imaging

Cost

Patient satisfaction

Search strategy

((((("Community-Acquired Infections"[MeSH Terms] OR ("community acquired"[All Fields] AND "infections"[All Fields]) OR "Community-Acquired Infections"[All Fields] OR ("community"[All Fields] AND "acquired"[All Fields] AND "infection"[All Fields]) OR "community acquired infection"[All Fields] OR "Community-Acquired Infections"[MeSH Terms]) AND ("pneumonia"[MeSH Terms] OR "pneumonia"[All Fields] OR "pneumonias"[All Fields] OR "pneumoniae"[All Fields] OR "pneumoniae s"[All Fields])) AND (("respiratory tract infections"[MeSH Terms] OR ("respiratory"[All Fields] AND "tract"[All Fields] AND "infections"[All Fields]) OR "respiratory tract infections"[All Fields]))) AND ((english[Filter]) AND (alladult[Filter]))) AND ((((("doppler ultrasound"[All Fields]) OR ("chest x ray"[All Fields])) OR ("chest radiograph"[All Fields])) OR (("Ultrasonography, Doppler"[Mesh]) OR ("Radiography, Thoracic"[Mesh]) OR (“diagnostic imaging, lung”[Mesh])) Filters: English, Adult: 19+ years

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Figure S1: Flow of information diagram

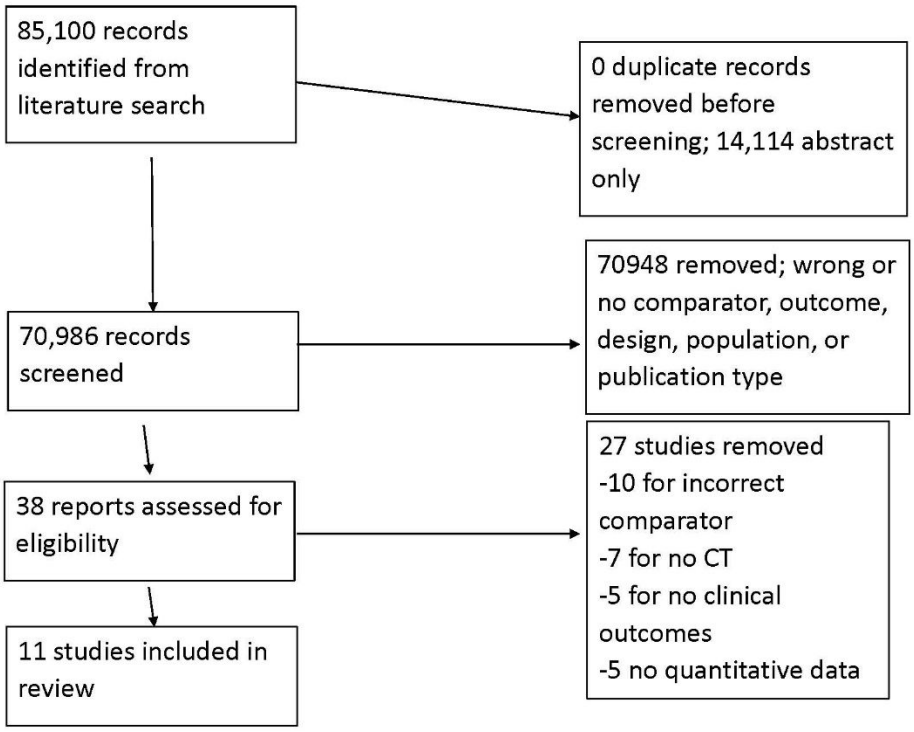

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Table S1: Studies selected

Study	Type of Study	Location	Number of Subjects	Population	Intervention	Outcomes	Risk of Bias
Amatya 2018	Observational	Nepal	62	Patients with suspected CAP and CT scan in ED[a]	Lung Ultrasound, CXR	Sensitivity, Specificity **	None
Bourcier 2014	Observational	France	144	Patients with suspected CAP and CT scan in ED[b]	Lung Ultrasound, CXR	Sensitivity, Specificity**	None
Cortallero 2012	Observational	Italy	120	Patients with suspected CAP and CT scan in ED[c]	Lung Ultrasound, CXR	Sensitivity, Specificity **	None
Dhawan 2022	Observational	India	85	Patients with suspected CAP and CT scan in tertiary care hospital ICUs[d]	Lung Ultrasound, CXR	Sensitivity, Specificity **	None
Gibbons 2021	Observational	USA	110	Patients with suspected CAP and CT scan in ED[e]	Lung Ultrasound, CXR	Sensitivity, Specificity **	None
Liu 2014	Observational	China	179	Patients with suspected CAP and CT scan in ED[f]	Lung Ultrasound, CXR	Sensitivity, Specificity **	None

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Corradi 2015	Observational	Italy	54	Patients with suspected CAP and CT scan in ED[g]	Lung Ultrasound, CXR	Sensitivity, Specificity **	None
Fares 2015	Observational	Egypt	38	Patients with suspected CAP and CT scan in a hospital ICU[h]	Lung Ultrasound, CXR	Sensitivity, Specificity **	None
Karimi 2019	Observational	Iran	280	Patients with suspected CAP and CT scan in ED[i]	Lung Ultrasound, CXR	Sensitivity, Specificity **	None
Taghizadieh 2015	Observational	Iran	30	Patients with suspected CAP and CT scan in ED[j]	Lung Ultrasound, CXR	Sensitivity, Specificity **	None
Bitar 2018	Observational	Kuwait	82	Patients with suspected CAP and CT scan in a hospital medical-surgical ICU[k]	Lung Ultrasound, CXR	Sensitivity, Specificity **	None

[a]Amatya Y, et al. Int J Emerg Med. 2018 Mar 12;11(1):8. Patients had at least three of the following signs or symptoms: temperature greater than 38 °C or history of fever, cough, dyspnea, tachypnea (respiratory rate greater than 20), or oxygen saturation lower than 92%.
[b]Bourcier JE, et al. Am J Emerg Med. 2014 Feb;32(2):115-8. At least three of the following items: tympanic temperature equal or higher than 38°C, cough, dyspnea, heart rate higher than 100 beats per minute, saturation of oxygen lower or equal to 92% in ambient air.
[c]Cortellaro F, et al. Emerg Med J. 2012 Jan;29(1):19-23wig S, Ruiz M, Mensa J, et al. Severe community-acquired pneumonia: assessment of severity criteria. Am J Respir Crit Care Med 1998;158:1102–1108. Signs and symptoms considered as suggestive of CAP were: cough; pleuritic pain; sputum production; fever; dyspnea.
[d]Dhawan J, et al. Indian J Crit Care Med. 2022 Aug;26(8):920-929. Clinical suspicion of pneumonia was considered when the following criteria was met: Symptoms suggestive of pneumonia (fever, cough, purulent sputum, and pleuritic chest pain), fulfilled minor criteria with at least three of the following symptoms: Respiratory rate >30 breaths/minute, PaO2/FiO2 <250, multilobar infiltrates, confusion/ disorientation, uremia [blood urea nitrogen (BUN) >20 mg/dL], leukopenia (WBC count <4,000 cells/mm3), thrombocytopenia (platelet count <100,000 cells/mm3),

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hypothermia (core temperature <36°C), and hypotension requiring aggressive fluid resuscitation; fulfilled major criteria with a requirement of at least one of the following factors: Invasive mechanical ventilation and septic shock with need for vasopressors.

[e]Gibbons RC, et al. J Emerg Med. 2021 May;60(5):615-625. Patients with one or more of the predefined signs and symptoms of COVID-19 were eligible for enrollment. Predefined signs and symptoms included: cough, fever, dyspnea, myalgia, malaise, ageusia, anosmia, increased work of breathing, temperature $ 38 _C (100.4 F), heartrate $ 100beats/ min, respiratory rate $ 16 breaths/min, and SpO2 < 94%.

[f]Liu XL, et al. Emerg Med J. 2015 Jun;32(6):433-8. Signs and symptoms considered as suggestive of CAP included: cough, pleuritic pain, sputum production, fever, dyspnea.

[g]Corradi F, et al. Biomed Res Int 2015:1-8. Pneumonia was clinically suspected on the basis of cough, dyspnea, body temperature >38◦C or <35◦C, heart rate >90 beats/min, tachypnea >20 breaths/min, rales or crackles on auscultation, and abnormal oxygen saturation.

[h]Fares Auf M-N. Med J Cairo Univ 2015;83:307–14. Pneumonia diagnosis based on suggestive history (fever, cough, sputum production, dyspnea).General and local physical signs suggestive of pneumonia.

[l]Karimi E. Arch Acad Emerg Med 2019;7:e8. clinical symptoms of pneumonia such as cough, phlegm, shortness of breath, hemoptysis, and temperature higher than 38±C.

[j]Taghizadieh A, et al.. Emerg 2015;3:114–6. Presence of fever, cough, pleuritic pain, sputum production, and dyspnea were considered as signs and symptoms of CAP.

[k]Bitar ZI, et al.. Health Sci Rep 2019;2:e102. The diagnosis of pneumonia was confirmed by a set of clinical features (clinical history and physical examination), microbiological testing for admitted patients (blood and sputum culture, legionella and pneumococcal urinary antigen testing, and multiplex polymerase chain reaction assay for detecting *Chlamydia pneumoniae, Mycoplasma pneumoniae*, and respiratory tract viruses), inflammatory markers (c-reactive protein >10 mg/L and procalcitonin ≥0.25 ng/mL), along with the presence of consolidation or opacification on a CXR or chest CT.

** - performance characteristics for CXR and LUS were calculated using CT scan results as reference standard.

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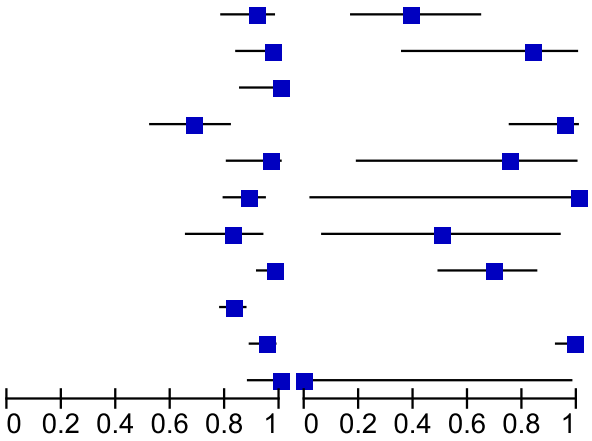
Figure S2: Forest plots

A) Analysis #1: Ultrasound (using chest CT scan as the reference standard)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Amatya 2018	40	11	4	7	0.91 [0.78, 0.97]	0.39 [0.17, 0.64]
Bitar 2019	31	1	1	5	0.97 [0.84, 1.00]	0.83 [0.36, 1.00]
Bourcier 2014	23	0	0	0	1.00 [0.85, 1.00]	Not estimable
Corradi 2015	30	1	14	19	0.68 [0.52, 0.81]	0.95 [0.75, 1.00]
Cortallero 2012	25	1	1	3	0.96 [0.80, 1.00]	0.75 [0.19, 0.99]
Dhawan 2022	74	0	10	1	0.88 [0.79, 0.94]	1.00 [0.03, 1.00]
Fares 2015	28	2	6	2	0.82 [0.65, 0.93]	0.50 [0.07, 0.93]
Gibbons 2021	79	9	2	20	0.98 [0.91, 1.00]	0.69 [0.49, 0.85]
Karimi 2019	232	0	48	0	0.83 [0.78, 0.87]	Not estimable
Liu 2014	106	1	6	66	0.95 [0.89, 0.98]	0.99 [0.92, 1.00]
Taghizadieh 2015	29	1	0	0	1.00 [0.88, 1.00]	0.00 [0.00, 0.97]



B) Analysis #2: Chest X-Ray (using chest CT scan as the reference standard)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Amatya 2018	32	9	12	9	0.73 [0.57, 0.85]	0.50 [0.26, 0.74]
Bitar 2019	5	5	27	1	0.16 [0.05, 0.33]	0.17 [0.00, 0.64]
Bourcier 2014	12	0	11	0	0.52 [0.31, 0.73]	Not estimable
Corradi 2015	28	4	16	16	0.64 [0.48, 0.78]	0.80 [0.56, 0.94]
Cortallero 2012	18	1	8	3	0.69 [0.48, 0.86]	0.75 [0.19, 0.99]
Dhawan 2022	58	1	26	0	0.69 [0.58, 0.79]	0.00 [0.00, 0.97]
Fares 2015	24	3	6	5	0.80 [0.61, 0.92]	0.63 [0.24, 0.91]
Gibbons 2021	57	13	24	16	0.70 [0.59, 0.80]	0.55 [0.36, 0.74]
Karimi 2019	263	0	17	0	0.94 [0.90, 0.96]	Not estimable
Liu 2014	87	4	25	63	0.78 [0.69, 0.85]	0.94 [0.85, 0.98]
Taghizadieh 2015	27	1	2	0	0.93 [0.77, 0.99]	0.00 [0.00, 0.97]

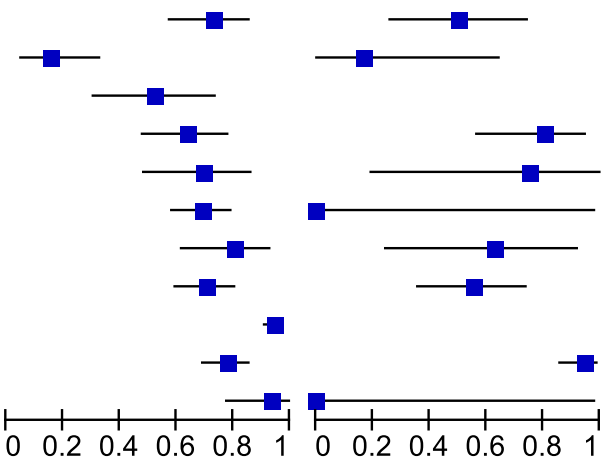


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Table S2: Evidence profile

Population: Adults with suspected CAP
Comparison: Chest x-ray versus lung ultrasound
Setting: Inpatients and outpatients

Quality assessment							Summary of Findings		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	# patients	Effect (range)		
Sensitivity and specificity: Ultrasound (using chest CT scan as the reference standard)										
11[1,2]	Accuracy	Not Serious	Serious[3]	Not serious[4,5]	Serious[6]	None	939	Sensitivity= median 95% (range 68-100%) Specificity= median 75%[6] (range 0-100%)	⊕⊕◯◯ LOW	CRITICAL
Sensitivity and specificity: Chest X-Ray (using chest CT scan as the reference standard)										
11[1,2]	Accuracy	Not Serious	Serious[5]	Not serious[4,5]	Serious[6]	None	939	Sensitivity= median 70% (range 16-94%) Specificity= median 55%[6] (range 0-94%)	⊕⊕◯◯ LOW	CRITICAL

Footnotes:

1. Amatya Y, et al. Int J Emerg Med. 2018 Mar 12;11(1):8.; Bitar ZI, et al. Health Sci Rep 2019;2:e102; Bourcier JE, et al. Am J Emerg Med. 2014 Feb;32(2):115-8.; Corradi F, et al. Biomed Res Int 2015:1-8; Cortellaro F, et al. Emerg Med J. 2012 Jan;29(1):19-23; Dhawan J, et al. Indian J Crit Care Med. 2022 Aug;26(8):920-929; Fares Auf M-N. Med J Cairo Univ 2015;83:307–14; Gibbons RC, et al. J Emerg Med. 2021 May;60(5):615-625; Karimi E. Arch Acad Emerg Med 2019;7:e8; Liu XL, et al. Emerg Med J. 2015 Jun;32(6):433-8; Taghizadieh A, et al. Emerg 2015;3:114–6.
2. Testa A, et al. Crit Care. 2012 Feb 17;16(1):R30 was excluded due to being judged an outlier.
3. Inconsistency: Wide range of sensitivity and specificity estimates across studies as seen in the Forest plots.
4. Indirectness of the comparison: The question asks about ultrasound compared to chest x-ray. However, the studies are accuracy studies that compared ultrasound to a reference standard and compared chest x-ray to a reference standard (i.e., chest CT). Therefore, answering the question requires an indirect comparison with an assumption of transitivity. The committee recognized the indirect nature of the comparison but judged that it did not further reduce its certainty in the estimates beyond the inconsistency and the imprecision.
5. Indirectness of the population: The question asks about patients with suspected CAP, but most of the studies enrolled patients with suspected CAP who also required a chest CT scan (usually due to discordant results between the chest x-ray and lung ultrasound). The committee recognized the indirectness of the population but judged that it did not further reduce its certainty in the estimates beyond the inconsistency and the imprecision.
6. Imprecision: Wide confidence intervals for individual studies as seen in the Forest plots.

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Table S3: EtD framework

QUESTION

Should lung ultrasound be considered a reasonable alternative to chest x-ray in patients with suspected community-acquired pneumonia?	
POPULATION:	Patients with suspected community-acquired pneumonia
INTERVENTION:	Lung ultrasound
COMPARATOR:	Chest x-ray
SETTING:	Inpatients and outpatients

ASSESSMENT

Test accuracy

How accurate are the tests?

JUDGEMENT	RESEARCH EVIDENCE
○ CXR is a lot more accurate ○ CXR is slightly more accurate ○ Lung US is a lot more accurate ○ Lung US is slightly more accurate ● Chest x-ray and US are comparably accurate	TEST CHARACTERISTICS The guideline committee judged the sensitivities and specificities of lung ultrasound and chest x-ray as comparable. The estimated medians might seem quite different but, when one considers that the lung ultrasound studies were likely performed by experienced operators, the committee concluded that the accuracy of lung ultrasound is likely overestimated in the studies compared with routine clinical practice. When one accounts for this likelihood, the committee concluded that the accuracy of lung ultrasound and chest x-ray are likely comparable. Lung ultrasound Sensitivity = median 95% (range 68-100%) Specificity = median 75% (range 0-100%) Chest x-ray Sensitivity = median 70% (range 16-94%) Specificity = median 55% (range 0-94%)

Desirable Effects

How substantial are the desirable effects of making a diagnosis? “Substantial” refers to both the importance and magnitude of the desirable effects. As an example, a small improvement in a critical outcome might be considered more substantial than a large improvement in an unimportant outcome.

JUDGEMENT	RESEARCH EVIDENCE
○ CXR is a lot more likely to lead to desirable effects ○ CXR is slightly more likely to lead to desirable effects ○ Lung US is a lot more likely to lead to desirable effects ○ Lung US is slightly more likely to lead to desirable effects ● Chest x-ray and US will lead to similar desirable effects	DESIRABLE PATIENT-IMPORTANT OUTCOMES Desirable effects derive from true positive and true negative results. They include the initiation or continuation of appropriate antibiotic therapy in those you have pneumonia, the elimination of the burdens and costs of seeking alternative diagnoses in those you have pneumonia, avoiding unnecessary antibiotic therapy in those who do not have pneumonia, and promoting ongoing pursuit of the correct diagnosis in those who do not have pneumonia. For both lung ultrasound and chest x-ray, a positive test result will result in the same intervention, antibiotics, and therefore eventually the same outcomes. Thus, the committee concluded that if test accuracy is comparable (see above), downstream desirable outcomes must also be comparable. Sensitivity = true positive rate:

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	Lung ultrasound = 95% Chest x-ray = 70% Specificity = true negative rate: Lung ultrasound = 75% Chest x-ray = 55%

Undesirable Effects

How substantial are the undesirable effects of making a diagnosis? "Substantial" refers to both the importance and magnitude of the undesirable effects. As an example, a small but important complication of diagnostic testing might be considered more substantial than a large but unimportant complication.

JUDGEMENT	RESEARCH EVIDENCE
○ CXR is a lot more likely to lead to undesirable effects ○ CXR is slightly more likely to lead to undesirable effects ○ Lung US is a lot more likely to lead to undesirable effects ○ Lung US is slightly more likely to lead to undesirable effects ● Chest x-ray and US will lead to similar undesirable effects	UNDESIRABLE PATIENT-IMPORTANT OUTCOMES Undesirable effects of diagnostic studies derive from false positive and false negative results. In this case, they include the initiation or continuation of inappropriate antibiotic therapy in those who test positive but do not have pneumonia, cessation of the pursuit of the correct diagnosis in those who test positive but do not have pneumonia, unnecessary additional diagnostic testing in those who test negative but have pneumonia, and delays in antibiotic therapy in those who test negative but have pneumonia. For both lung ultrasound and chest x-ray, a negative test result will result in the same actions (foregoing or discontinuing antibiotics, additional diagnostic testing to either confirm the negative result or seek an alternative diagnosis). Thus, the committee concluded that if test accuracy is comparable (see above), downstream undesirable outcomes must also be comparable. 1 - sensitivity = false negative rate: Lung ultrasound = 5% Chest x-ray = 30% 1 - specificity = false positive rate: Lung ultrasound = 25% Chest x-ray = 45%

Balance of desirable and undesirable effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE
○ Favors chest x-ray ○ Probably favors chest x-ray ● Does not favor either chest x-ray or lung ultrasound ○ Favors lung ultrasound ○ Probably favors lung ultrasound ○ Varies ○ Don't know	The guideline committee noted that chest x-ray and lung ultrasound probably lead to similar desirable and undesirable effects (see above). Therefore, they concluded that the balance of effects does not favor either chest x-ray or lung ultrasound.

Quality of evidence of test accuracy

What is the committee's confidence in the above listed estimates of test accuracy (i.e., what is the quality of evidence)?

JUDGEMENT	RESEARCH EVIDENCE

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○ Very low ● Low ○ Moderate ○ High ○ No included studies	QUALITY OF EVIDENCE The quality of evidence for both lung ultrasound and chest x-rays was low because there are accuracy studies that were downgraded due to inconsistency (there were a wide range of estimates across studies) and imprecision (the confidence intervals were wide for most studies).

Quality of evidence of test result/management

What is the committee's confidence that the test results will lead to certain clinical actions?

JUDGEMENT	RESEARCH EVIDENCE
○ Very low ○ Low ○ Moderate ○ High ● No included studies	The committee did not evaluate published evidence regarding clinical actions that follow lung ultrasound and chest x-ray results. The committee concluded that the frequency of clinical actions following lung ultrasound and chest x-ray must be comparable if accuracy of studies is comparable (see above) since the tests lead to the same clinical actions. Clinical actions include the initiation/continuation antibiotic therapy or foregoing/discontinuing antibiotic therapy.

Quality of evidence of management/clinical outcomes

What is the committee's confidence that the clinical actions prompted by the test results will lead to certain outcomes?

JUDGEMENT	RESEARCH EVIDENCE
○ Very low ○ Low ○ Moderate ○ High ● No included studies	The committee did not evaluate published evidence regarding the clinical outcomes of antibiotic therapy in patients with CAP. However, the committee was confident that antibiotic therapy improves clinical outcomes in patients with CAP. The committee therefore concluded that clinical outcomes following lung ultrasound and chest x-ray must be comparable if the accuracy of studies is comparable (see above), since the tests lead to the same clinical actions which create those outcomes.

Quality of evidence

What is the overall certainty of the effects of the tests? This is defined as the lowest quality of evidence among the qualities of evidence of test accuracy, result/management, and management/clinical outcomes

JUDGEMENT	RESEARCH EVIDENCE
● Very low ○ Low ○ Moderate ○ High ○ No included studies	The overall quality of evidence is very low because, even if there exists good evidence that test results effect clinical actions that improve outcomes, there is very low quality of evidence for test accuracy for both lung ultrasound and chest x-ray.

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	Lung ultrasound and chest x-ray are non-invasive, painless, and not burdensome. Therefore, both are acceptable to most patients. This conclusion is based on the committee's non-systematic clinical observations.

Feasibility

Is the intervention feasible to implement?

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JUDGEMENT	RESEARCH EVIDENCE
○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know	Both chest x-ray and lung ultrasound are available in most clinical settings. The primary limiting factor is the availability of experience operators and interpreters of lung ultrasound. This conclusion is based on the committee's non-systematic clinical observations.

SUMMARY OF JUDGMENTS

	JUDGEMENT						
TEST ACCURACY	CXR a lot more	CXR slightly more	**CXR and lung US are comparable**	Lung US slightly more	Lung US a lot more	-	-
DESIRABLE EFFECTS	CXR a lot more	CXR slightly more	**CXR and lung US are comparable**	Lung US slightly more	Lung US a lot more	-	-
UNDESIRABLE EFFECTS	CXR a lot more	CXR slightly more	**CXR and lung US are comparable**	Lung US slightly more	Lung US a lot more	-	-
BALANCE OF EFFECTS	Favors CXR	Probably favors CXR	**Does not favor either CXR or lung US**	Probably favors lung US	Favors lung US	Varies	Don't know
QUALITY OF EVIDENCE OF TEST ACCURACY	Very low	**Low**	Moderate	High	No included studies	-	-
QUALITY OF EVIDENCE OF TEST RESULT/MANAGEMENT	Very low	Low	Moderate	**High**	**No included studies**	-	-
QUALITY OF EVIDENCE OF MANAGEMENT/OUTCOMES	Very low	Low	Moderate	High	**No included studies**	-	-
QUALITY OF EVIDENCE	Very low	**Low**	Moderate	High	No included studies	-	-
ACCEPTABILITY	No	Probably no	Probably yes	**Yes**	Varies	Don't know	-
FEASIBILITY	No	Probably no	**Probably yes**	Yes	Varies	Don't know	-

TYPE OF RECOMMENDATION

Strong recommendation for chest x-ray	Conditional recommendation for chest x-ray	Conditional recommendation for either chest x-ray or lung ultrasound	Conditional recommendation for lung ultrasound	Strong recommendation for lung ultrasound
○	○	●	○	○

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CONCLUSIONS

Recommendation

For patients with suspected community-acquired pneumonia, we suggest that lung ultrasound be considered an acceptable alternative to chest x-rays in medical centers where the appropriate expertise exists (conditional recommendation, low quality of evidence).

Participation = 15/18 (83%)
Strong recommendation for chest x-ray = 0/15 (0%).
Conditional recommendation for chest x-ray =1/15 (6.67%).
Strong recommendation for lung ultrasound = 0/15 (0%).
Condition recommendation for lung ultrasound = 1/15 (6.67%).
Conditional recommendation for either chest x-ray or lung ultrasound = 13/15 (86.67%).

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PICO Question #2: Antibacterial therapy for CAP if a test for a respiratory virus is positive

Population: Adult CAP patients who test positive for a respiratory virus,
Intervention: Antibacterial therapy,
Comparator: No antibacterial therapy.
Outcomes:

Critical

Mortality (i.e. in-hospital, 28 day, 30 day, 60 day, 90 day, 180 day, <7% at 10 days)

Length of stay (i.e. hospital)

Treatment failure (i.e. decompensation, need for hospital admission, reasmission need for mechanical ventilation, need for vasopressor support, ICU transfer)

Clinical stability

Important

Antibiotic-associated adverse events (inc side effects and resistant organisms)

Secondary infection

Days of antibiotics

Return to function (work, exertion, home after hospitalization) or quality of life

Symptoms (i.e. total number, etc)

Cost

Search Strategy

Overall Question #1

((("antibiotic"[Title/Abstract]) OR (("Anti-Bacterial Agents"[Mesh]) OR "Anti-Bacterial Agents" [Pharmacological Action])) AND ((("Community-Acquired Infections"[MeSH Terms] OR ("community acquired"[All Fields] AND "infections"[All Fields]) OR "Community-Acquired Infections"[All Fields] OR ("community"[All Fields] AND "acquired"[All Fields] AND "infection"[All Fields]) OR "community acquired infection"[All Fields] OR "Community-Acquired Infections"[MeSH Terms]) AND ("pneumonia"[MeSH Terms] OR "pneumonia"[All Fields] OR "pneumonias"[All Fields] OR "pneumoniae"[All Fields] OR "pneumoniae s"[All Fields])) AND (("respiratory tract infections"[MeSH Terms] OR ("respiratory"[All Fields] AND "tract"[All Fields] AND "infections"[All Fields]) OR "respiratory tract infections"[All Fields]))))

Overall Question #1

(("communal"[All Fields] OR "communalism"[All Fields] OR "communalities"[All Fields] OR "communality"[All Fields] OR "communally"[All Fields] OR "commune"[All Fields] OR "communes"[All Fields] OR "community s"[All Fields] OR "communitys"[All Fields] OR "residence characteristics"[MeSH Terms] OR ("residence"[All Fields] AND "characteristics"[All Fields]) OR "residence characteristics"[All

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Fields] OR "communities"[All Fields] OR "community"[All Fields]) AND ("acquirable"[All Fields] OR "acquire"[All Fields] OR "acquired"[All Fields] OR "acquirement"[All Fields] OR "acquirements"[All Fields] OR "acquires"[All Fields] OR "acquiring"[All Fields]) AND ("pneumonia"[MeSH Terms] OR "pneumonia"[All Fields] OR "pneumonias"[All Fields] OR "pneumoniae"[All Fields] OR "pneumoniae s"[All Fields]) AND ("eur med j respir"[Journal] OR "respiratory"[All Fields]) AND ("virally"[All Fields] OR "virals"[All Fields] OR "virology"[MeSH Terms] OR "virology"[All Fields] OR "viral"[All Fields]) AND ("anti bacterial agents"[Pharmacological Action] OR "anti bacterial agents"[MeSH Terms] OR ("anti bacterial"[All Fields] AND "agents"[All Fields]) OR "anti bacterial agents"[All Fields] OR "antibiotic"[All Fields] OR "antibiotics"[All Fields] OR "antibiotic s"[All Fields] OR "antibiotical"[All Fields])) AND ((english[Filter]) AND (alladult[Filter]))

Indirect questions

((("antibiotic"[Title/Abstract]) OR (("Anti-Bacterial Agents"[Mesh]) OR "Anti-Bacterial Agents"[Pharmacological Action])) AND ((("Community-Acquired Infections"[MeSH Terms] OR ("community acquired"[All Fields] AND "infections"[All Fields]) OR "Community-Acquired Infections"[All Fields] OR ("community"[All Fields] AND "acquired"[All Fields] AND "infection"[All Fields]) OR "community acquired infection"[All Fields] OR "Community-Acquired Infections"[MeSH Terms]) AND ("pneumonia"[MeSH Terms] OR "pneumonia"[All Fields] OR "pneumonias"[All Fields] OR "pneumoniae"[All Fields] OR "pneumoniae s"[All Fields])) AND (("respiratory tract infections"[MeSH Terms] OR ("respiratory"[All Fields] AND "tract"[All Fields] AND "infections"[All Fields]) OR "respiratory tract infections"[All Fields] AND "anti bacterial agents/administration and dosage"[MeSH Terms]))))

Indirect population for Bronchitis

("antibiotic"[Title/Abstract] OR ("Anti-Bacterial Agents"[MeSH Terms] OR "Anti-Bacterial Agents"[Pharmacological Action])) AND (("Community-Acquired Infections"[MeSH Terms] OR ("community acquired"[All Fields] AND "infections"[All Fields]) OR "Community-Acquired Infections"[All Fields] OR ("community"[All Fields] AND "acquired"[All Fields] AND "infection"[All Fields]) OR "community acquired infection"[All Fields] OR "Community-Acquired Infections"[MeSH Terms]) AND ("bronchitis"[MeSH Terms] OR "bronchitis"[All Fields] OR "bronchitides"[All Fields]) AND ("respiratory tract infections"[MeSH Terms] OR ("respiratory"[All Fields] AND "tract"[All Fields] AND "infections"[All Fields]) OR "respiratory tract infections"[All Fields]))

Bronchitis

(("bronchitis"[MeSH Terms] OR "bronchitis"[All Fields] OR "bronchitides"[All Fields]) AND ("eur med j respir"[Journal] OR "respiratory"[All Fields]) AND ("virally"[All Fields] OR "virals"[All Fields] OR "virology"[MeSH Terms] OR "virology"[All Fields] OR "viral"[All Fields]) AND ("anti bacterial agents"[Pharmacological Action] OR "anti bacterial agents"[MeSH Terms] OR ("anti bacterial"[All Fields] AND "agents"[All Fields]) OR "anti bacterial agents"[All Fields] OR "antibiotic"[All Fields] OR "antibiotics"[All Fields] OR "antibiotic s"[All Fields] OR "antibiotical"[All Fields])) AND ((english[Filter]) AND (alladult[Filter]))

Indirect population for Tracheobronchitis

("antibiotic"[Title/Abstract] OR ("Anti-Bacterial Agents"[MeSH Terms] OR "Anti-Bacterial Agents"[Pharmacological Action])) AND (("Community-Acquired Infections"[MeSH Terms] OR

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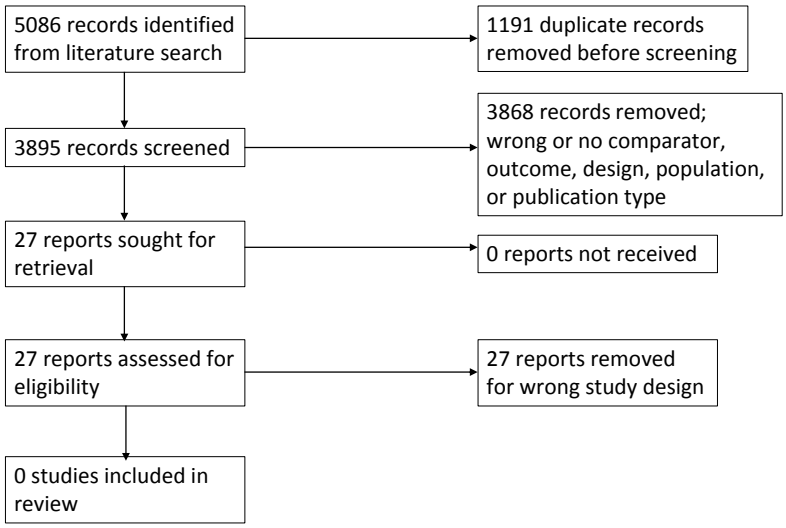
("community acquired"[All Fields] AND "infections"[All Fields]) OR "Community-Acquired Infections"[All Fields] OR ("community"[All Fields] AND "acquired"[All Fields] AND "infection"[All Fields]) OR "community acquired infection"[All Fields] OR "Community-Acquired Infections"[MeSH Terms]) AND ("tracheobronchitis"[All Fields]) AND ("respiratory tract infections"[MeSH Terms] OR ("respiratory"[All Fields] AND "tract"[All Fields] AND "infections"[All Fields]) OR "respiratory tract infections"[All Fields]))

Tracheobronchitis

("tracheobronchitis"[All Fields] AND (("eur med j respir"[Journal] OR "respiratory"[All Fields]) AND ("virally"[All Fields] OR "virals"[All Fields] OR "virology"[MeSH Terms] OR "virology"[All Fields] OR "viral"[All Fields])) AND ("anti bacterial agents"[Pharmacological Action] OR "anti bacterial agents"[MeSH Terms] OR ("anti bacterial"[All Fields] AND "agents"[All Fields]) OR "anti bacterial agents"[All Fields] OR "antibiotic"[All Fields] OR "antibiotics"[All Fields] OR "antibiotic s"[All Fields] OR "antibiotical"[All Fields])) AND ((english[Filter]) AND (alladult[Filter]))

Figure S3: Flow of information diagram



Forest Plots

None

Evidence Profile

There are no studies (randomized or non-randomized) concerning CAP as diagnosed by signs, symptoms, and imaging that compare an antibiotic to no antibiotic regimen following the identification of a respiratory viral pathogen. Therefore, an evidence profile and evidence-to-decision table were not created. The committee informed its recommendations with non-comparative evidence and non-systematic clinical observations. In published investigations, the decision to continue or discontinue antibiotics after finding a viral pathogen included other considerations such as the likelihood of bacterial coinfection depending on the specific virus identified, the difficulty in excluding concomitant bacterial infections with available diagnostic techniques, and clinical stability of the patient.

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PICO question #3: Antibiotic duration for CAP

Population: Adult patients with community acquired pneumonia

Intervention: Less than five days of antibiotics

Comparator: Five or more days of antibiotics

Outcomes

Critical

Mortality

Treatment success/failure

CAP-related complications

Important

Duration of hospitalization

Antibiotic-free days

Patient experience

Cost

Antibiotic resistance

Search Strategy

1. ("Pneumonia, Bacterial"[Mesh] OR "Pneumonia"[Mesh] OR "Chlamydial Pneumonia"[Mesh] OR "Pneumonia, Viral"[Mesh] OR "Pneumonia, Staphylococcal"[Mesh] OR "Pneumonia, Mycoplasma"[Mesh] OR "Pneumonia, Pneumococcal"[Mesh] OR "Respiratory Tract Infections"[Mesh]) AND ("Community-Acquired Infections"[Mesh]) AND ("anti bacterial agents"[Pharmacological Action] OR "anti bacterial agents"[MeSH Terms] OR ("anti bacterial"[All Fields] AND "agents"[All Fields]) OR "anti bacterial agents"[All Fields] OR "antibiotic"[All Fields] OR "antibiotics"[All Fields] OR "antibiotics"[All Fields] OR "antibiotical"[All Fields] OR "antibacterial agents"[Pharmacological Action] OR "anti bacterial agents"[MeSH Terms] OR ("anti bacterial"[All Fields] AND "agents"[All Fields]) OR "antibacterial agents"[All Fields] OR "antibacterial"[All Fields] OR "antibacterials"[All Fields] OR "antibacterially"[All Fields])) OR "Therapeutics"[Mesh] OR "therapy" [Subheading]) AND ("Duration of Therapy"[Mesh])
2. AND (English[Language]) AND (humans[Filter]) NOT ("infant"[mesh] OR "child"[mesh] OR adolescent"[mesh])
3. ("Pneumonia, Bacterial"[Mesh]) AND "Duration of Therapy"[Mesh]

Community acquired pneumonia treatment duration

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4. Reference search of other identified studies

Figure S4: Flow of information diagram

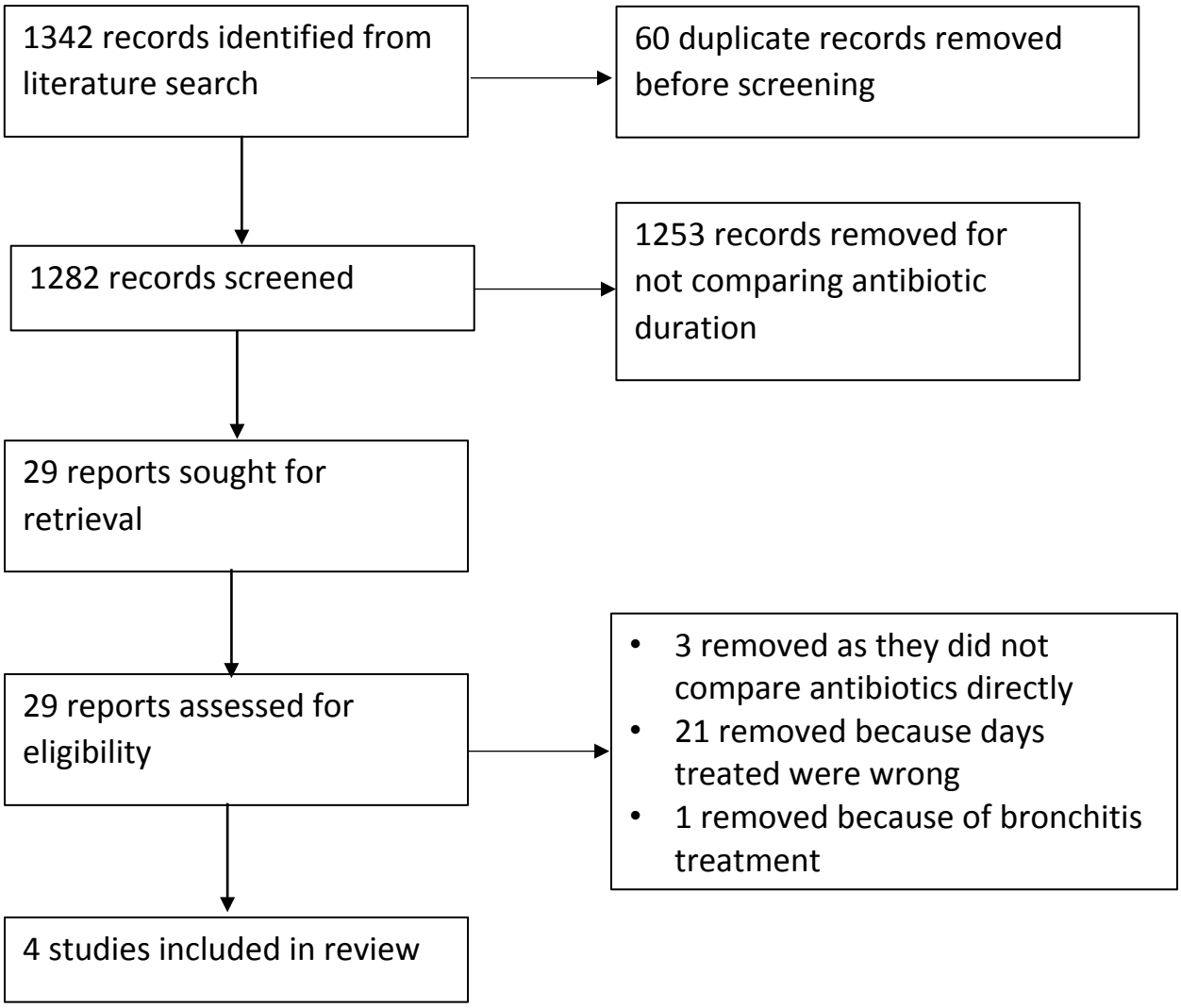

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Table S4: Studies selected

Study	Type of study	Location	Number of subjects (I/C)	Population	Outcomes
[1]**El Moussaoui - 2006**	RCT	Netherlands	119 (56/63)	Inpatients	Clinical cure
[2]**D'Ignazio – 2004**	RCT	Worlwide (Canada, Chile, India, Lithuania, Mexico, Peru, Russia, and United States)	363 (174/189)	Outpatients	Clinical cure
[3]**Dinh - 2021**	RCT	France	310 (157/153)	Inpatients	Mortality, clinical cure, length of stay
[4]**Drehobl - 2005**	RCT	Worldwide (United States, Canada, Argentina, Russia, India, Estonia, and Lithuania)	411 (202/209)	Outpatients	Clinical cure

RCT=randomized controlled trial; I=intervention; C=control

1. el Moussaoui, R., de Borgie, C. A., van den Broek, P., Hustinx, W. N., Bresser, P., van den Berk, G. E., Poley, J. W., van den Berg, B., Krouwels, F. H., Bonten, M. J., Weenink, C., Bossuyt, P. M., Speelman, P., Opmeer, B. C., Prins, J. M.. Effectiveness of discontinuing antibiotic treatment after three days versus eight days in mild to moderate-severe community acquired pneumonia: randomised, double blind study. Bmj; Jun 10 2006.
2. D'Ignazio, J., Camere, M. A., Lewis, D. E., Jorgensen, D., Breen, J. D.. Novel, single-dose microsphere formulation of azithromycin versus 7-day levofloxacin therapy for treatment of mild to moderate community-acquired Pneumonia in adults. Antimicrob Agents Chemother; Oct 2005
3. Dinh, A., Ropers, J., Duran, C., Davido, B., Deconinck, L., Matt, M., Senard, O., Lagrange, A., Makhloufi, S., Mellon, G., de Lastours, V., Bouchand, F., Mathieu, E., Kahn, J. E., Rouveix, E., Grenet, J., Dumoulin, J., Chinet, T., Pépin, M., Delcey, V., Diamantis, S., Benhamou, D., Vitrat, V., Dombret, M. C., Renaud, B., Perronne, C., Claessens, Y. E., Labarère, J., Bedos, J. P., Aegerter, P., Crémieux, A. C.. Discontinuing β-lactam treatment after 3 days for patients with community-acquired pneumonia in non-critical care wards (PTC): a double-blind, randomised, placebo-controlled, non-inferiority trial. Lancet; Mar 27 2021.
4. Drehobl, M. A., De Salvo, M. C., Lewis, D. E., Breen, J. D.. Single-dose azithromycin microspheres vs clarithromycin extended release for the treatment of mild-to-moderate community-acquired pneumonia in adults. Chest; Oct 2005.

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Table S5: Study Interventions

Study	Antibiotics (I VS C)	Intervention days	Control days
Inpatient			
[1]El Moussaoui - 2006	Patients who improved after 3 days of IV amoxicillin were randomized to placebo or 750 mg of oral amoxicillin TID	3	8
[2]Dinh - 2021	After 72 hours of beta-lactam treatment, patients were randomized to receive placebo or 500 mg amoxicillin plus 62.5 mg of clavulanate TID	3	8
Outpatient			
[3]D'Ignazio – 2004	A single 2 gm dose azithromycin microspheres vs 500 mg oral levofloxacin	1	7
[4]Drehobl - 2005	A single 2 gm dose azithromycin microspheres vs clarithromycin	1	7

I=intervention; C=control; TID=three times daily

1. el Moussaoui, R., de Borgie, C. A., van den Broek, P., Hustinx, W. N., Bresser, P., van den Berk, G. E., Poley, J. W., van den Berg, B., Krouwels, F. H., Bonten, M. J., Weenink, C., Bossuyt, P. M., Speelman, P., Opmeer, B. C., Prins, J. M.. Effectiveness of discontinuing antibiotic treatment after three days versus eight days in mild to moderate-severe community acquired pneumonia: randomised, double blind study. Bmj; Jun 10 2006.
2. Dinh, A., Ropers, J., Duran, C., Davido, B., Deconinck, L., Matt, M., Senard, O., Lagrange, A., Makhloufi, S., Mellon, G., de Lastours, V., Bouchand, F., Mathieu, E., Kahn, J. E., Rouveix, E., Grenet, J., Dumoulin, J., Chinet, T., Pépin, M., Delcey, V., Diamantis, S., Benhamou, D., Vitrat, V., Dombret, M. C., Renaud, B., Perronne, C., Claessens, Y. E., Labarère, J., Bedos, J. P., Aegerter, P., Crémieux, A. C.. Discontinuing β-lactam treatment after 3 days for patients with community-acquired pneumonia in non-critical care wards (PTC): a double-blind, randomised, placebo-controlled, non-inferiority trial. Lancet; Mar 27 2021.
3. D'Ignazio, J., Camere, M. A., Lewis, D. E., Jorgensen, D., Breen, J. D.. Novel, single-dose microsphere formulation of azithromycin versus 7-day levofloxacin therapy for treatment of mild to moderate community-acquired Pneumonia in adults. Antimicrob Agents Chemother; Oct 2005
4. Drehobl, M. A., De Salvo, M. C., Lewis, D. E., Breen, J. D.. Single-dose azithromycin microspheres vs clarithromycin extended release for the treatment of mild-to-moderate community-acquired pneumonia in adults. Chest; Oct 2005.

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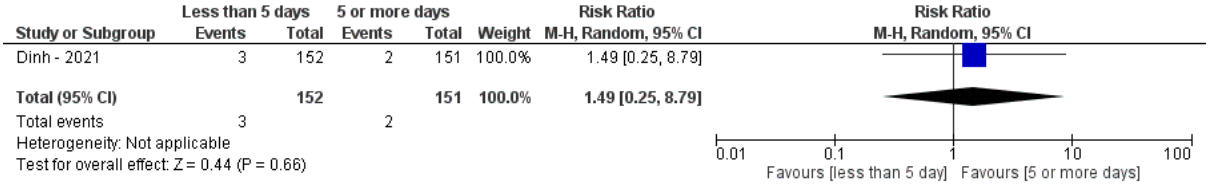
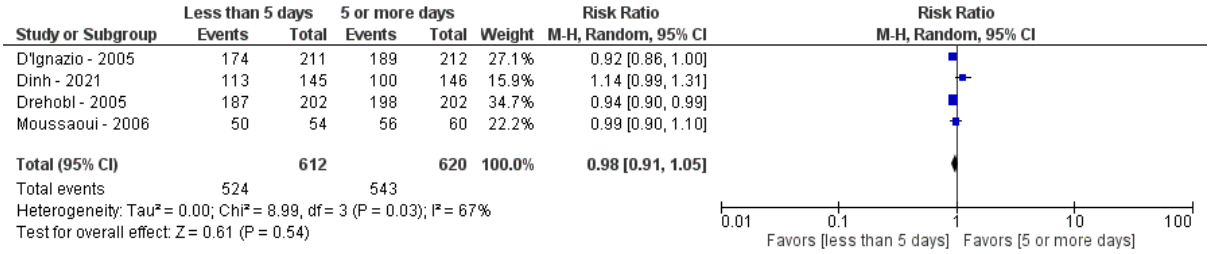
Figure S5: Forest Plots

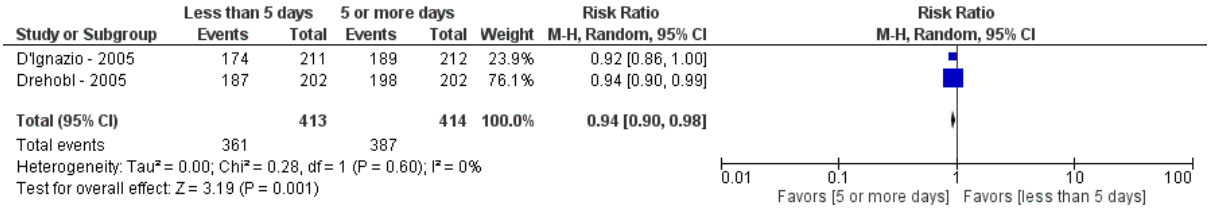
A) Analysis #1: Overall all-cause mortality



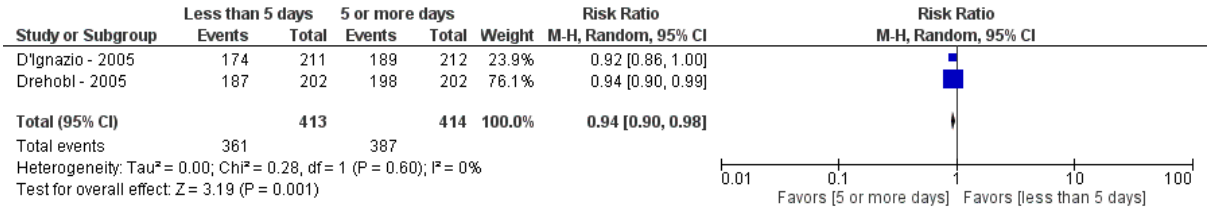
B) Analysis #2: Clinical cure – short follow-up (1-2 weeks)



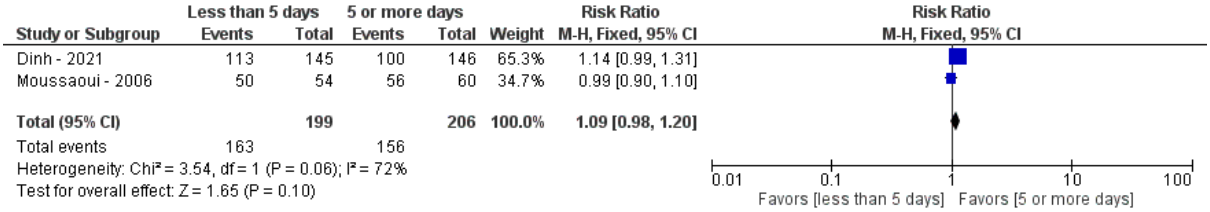
C) Sub-analysis #2.1: Clinical cure – short follow-up: azithromycin only



D) Sub-analysis #2.2: Clinical cure – short follow-up: outpatient only



E) Sub-analysis #2.3: Clinical cure – short follow-up: inpatient only



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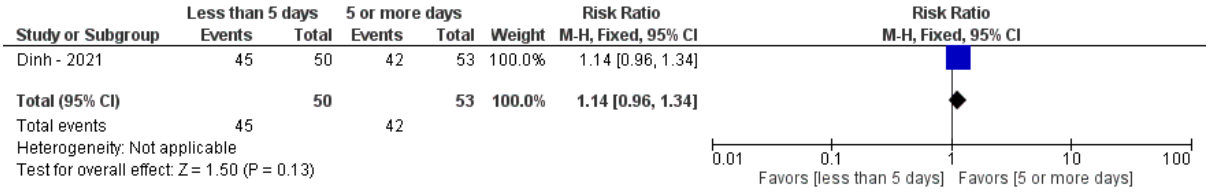
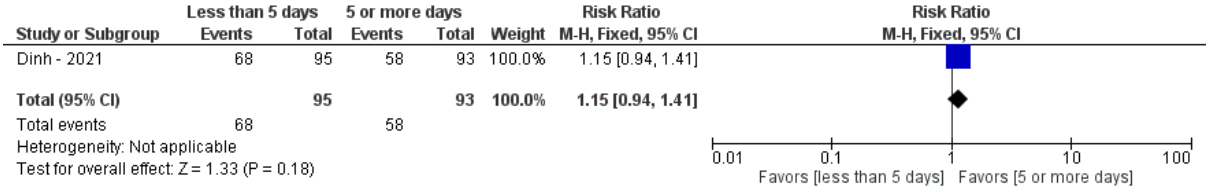
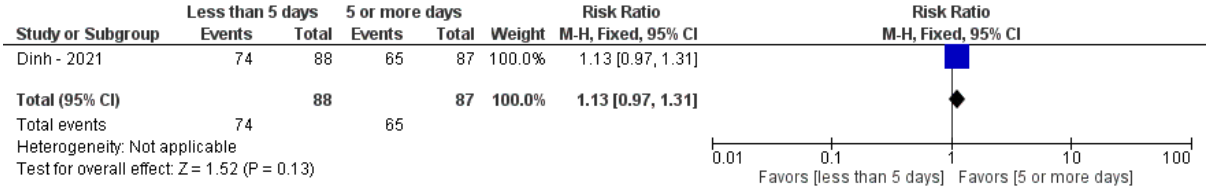
F) Sub-analysis #2.4: Clinical cure – short follow-up: PSI score <71



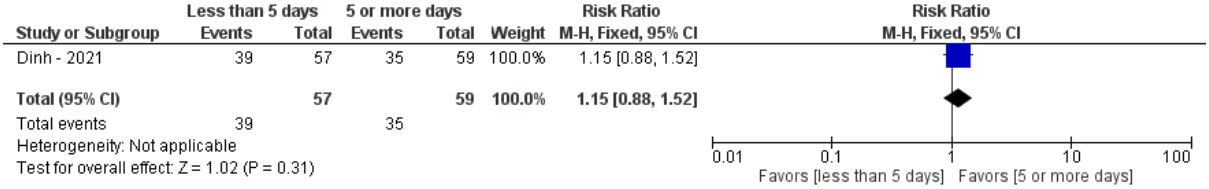
G) Sub-analysis #2.5: Clinical cure – short follow-up: PSI score >70



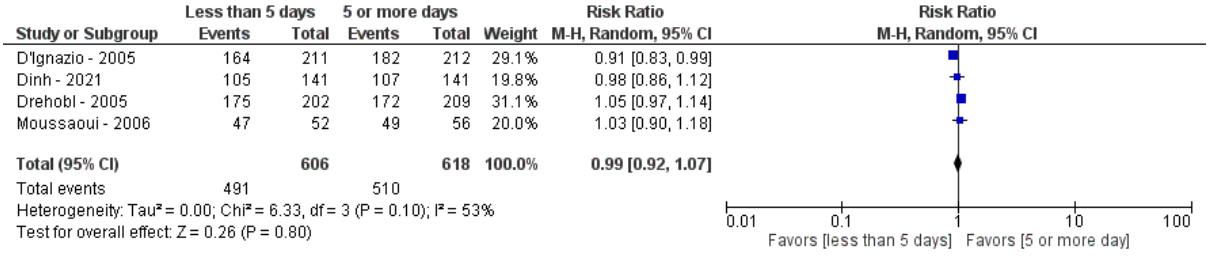
H) Sub-analysis #2.6: Clinical cure – short follow-up: PSI score <91



I) Sub-analysis #2.7: Clinical cure – short follow-up: PSI score >90



J) Analysis #3: Clinical cure – long follow-up (3-4 weeks)



K) Sub-analysis #3.1: Clinical cure – long follow-up: azithromycin only

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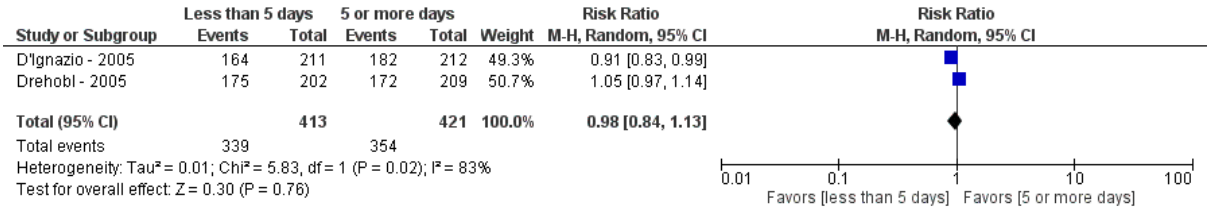
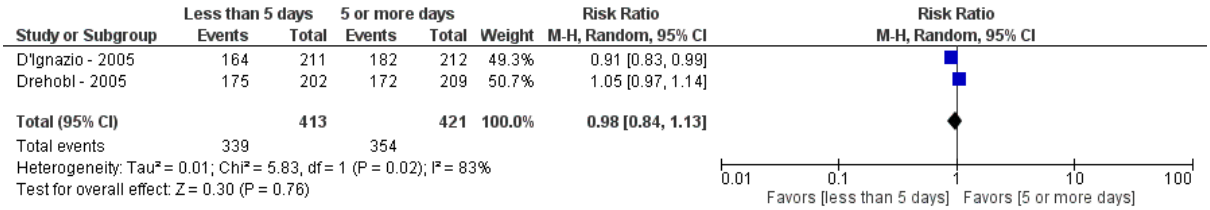
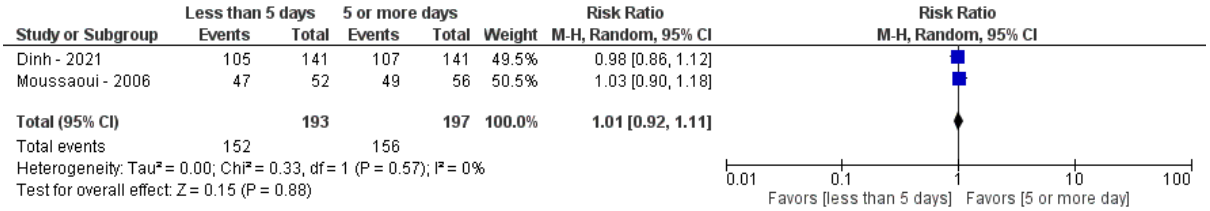


L) Sub-analysis #3.2: Clinical cure – long follow-up: outpatient only



M) Sub-analysis #3.3: Clinical cure – long follow-up: inpatient only



N) Analysis #4: Hospital length of stay

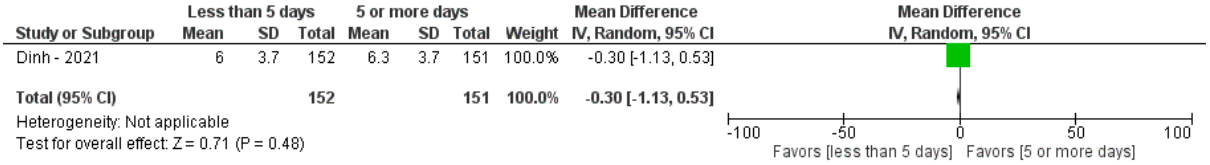


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Table S6: Evidence Profiles

Table S6.1
Population: Adult outpatients and inpatients with CAP who reach clinical stability
Comparison: Less than five days of antibiotics versus five or more days of antibiotics
Setting: All patients (outpatients and inpatients)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	less than 5 days	5 or more days	Relative (95% CI)	Absolute (95% CI)		
Clinical cure rate at 1-2 weeks												
4[1,2,3,4]	RCT	Not serious[5]	Serious[6]	Not serious	Serious[7]	none	524/612 (85.6%)	543/620 (87.6%)	RR 0.98 (0.91 to 1.05)	18 fewer per 1,000 (from 79 fewer to 44 more)	⊕⊕◯◯ Low	CRITICAL
Clinical cure rate at 3-4 weeks												
4[1,2,3,4]	RCT	Not serious[5]	Serious[6]	Not serious	Serious[7]	none	491/606 (81.0%)	510/618 (82.5%)	RR 0.99 (0.92 to 1.07)	8 fewer per 1,000 (from 66 fewer to 58 more)	⊕⊕◯◯ Low	CRITICAL

CI: confidence interval; RCT: randomized controlled trial; RR: risk ratio
Footnotes:

1. el Moussaoui, R., de Borgie, C. A., van den Broek, P., Hustinx, W. N., Bresser, P., van den Berk, G. E., Poley, J. W., van den Berg, B., Krouwels, F. H., Bonten, M. J., Weenink, C., Bossuyt, P. M., Speelman, P., Opmeer, B. C., Prins, J. M.. Effectiveness of discontinuing antibiotic treatment after three days versus eight days in mild to moderate-severe community acquired pneumonia: randomised, double blind study. Bmj; Jun 10 2006.
2. Drehobl, M. A., De Salvo, M. C., Lewis, D. E., Breen, J. D.. Single-dose azithromycin microspheres vs clarithromycin extended release for the treatment of mild-to-moderate community-acquired pneumonia in adults. Chest; Oct 2005.
3. Dinh, A., Ropers, J., Duran, C., Davido, B., Deconinck, L., Matt, M., Senard, O., Lagrange, A., Makhloufi, S., Mellon, G., de Lastours, V., Bouchand, F., Mathieu, E., Kahn, J. E., Rouveix, E., Grenet, J., Dumoulin, J., Chinet, T., Pépin, M., Delcey, V., Diamantis, S., Benhamou, D., Vitrat, V., Dombret, M. C., Renaud, B., Perronne, C., Claessens, Y. E., Labarère, J., Bedos, J. P., Aegerter, P., Crémieux, A. C.. Discontinuing β-lactam treatment after 3 days for patients with community-acquired pneumonia in non-critical care wards (PTC): a double-blind, randomised, placebo-controlled, non-inferiority trial. Lancet; Mar 27 2021.
4. D'Ignazio, J., Camere, M. A., Lewis, D. E., Jorgensen, D., Breen, J. D.. Novel, single-dose microsphere formulation of azithromycin versus 7-day levofloxacin therapy for treatment of mild to moderate community-acquired Pneumonia in adults. Antimicrob Agents Chemother; Oct 2005.

5. Risk of bias: Studies with minor protocol violations judged insufficient to warrant downgrading.
6. Inconsistency: Significant heterogeneity (defined as p-het <0.05 or $I^2 > 50\%$).
7. Imprecision: Wide confidence intervals, the ends of the confidence interval are likely to lead to different courses of action.

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Table S6.2
Population: Adult outpatients with CAP who reach clinical stability
Comparison: Less than five days of antibiotics versus five or more days of antibiotics
Setting: Outpatients

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	less than 5 days	5 or more days	Relative (95% CI)	Absolute (95% CI)		
Clinical cure rate at 1-2 weeks												
2[1,2]	RCT	Not serious[3]	Not serious	Not serious	Not serious	none	361/413 (87.4%)	~~387/414 (93.5%)~~ 387/421 (91.9%)	~~RR 0.94 (0.90 to 0.98)~~ RR 0.96 (0.91 to 1.01)	~~56 fewer per 1,000 (from 93 fewer to 19 fewer)~~ 45 fewer per 1,000 (from 87 fewer to 10 more)	⨁◯◯◯ Moderate	CRITICAL
Clinical cure rate at 3-4 weeks												
2[1,2]	RCT	Not serious[3]	Serious[4]	Not serious	Serious[5]	none	339/413 (82.1%)	354/421 (84.1%)	RR 0.98 (0.84 to 1.13)	17 fewer per 1,000 (from 135 fewer to 109 more)	⨁⨁◯◯ Low	CRITICAL

CI: confidence interval; RCT: randomized controlled trial; RR: risk ratio
Footnotes:

1. Drehobl, M. A., De Salvo, M. C., Lewis, D. E., Breen, J. D.. Single-dose azithromycin microspheres vs clarithromycin extended release for the treatment of mild-to-moderate community-acquired pneumonia in adults. Chest; Oct 2005.
2. D'Ignazio, J., Camere, M. A., Lewis, D. E., Jorgensen, D., Breen, J. D.. Novel, single-dose microsphere formulation of azithromycin versus 7-day levofloxacin therapy for treatment of mild to moderate community-acquired Pneumonia in adults. Antimicrob Agents Chemother; Oct 2005.
3. Risk of bias: Studies with minor protocol violations judged insufficient to warrant downgrading.
4. Inconsistency: Significant heterogeneity (defined as p-het <0.05 or I^2 > 50%).
5. Imprecision: Wide confidence intervals, the ends of the confidence interval are likely to lead to different courses of action.

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Table S6.3
Population: Adult inpatients with CAP who reach clinical stability
Comparison: Less than five days of antibiotics versus five or more days of antibiotics
Setting: Inpatients

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	less than 5 days	5 or more days	Relative (95% CI)	Absolute (95% CI)		
Overall mortality												
1[1]	RCT	Not serious[2]	Not serious	Not serious	Serious[3]	none	17/535 (3.2%)	18/371 (4.9%)	RR 0.63 (0.27 to 1.49)	18 fewer per 1,000 (from 35 fewer to 24 more)	⨁◯◯◯ Moderate	CRITICAL
Clinical cure rate at 1-2 weeks												
2[1,4]	RCT	Not serious[2]	Serious[5]	Not serious	Serious[3]	none	163/199 (81.9%)	156/206 (75.7%)	RR 1.06 (0.90 to 1.24)	45 more per 1,000 (from 76 fewer to 182 more)	⨁⨁◯◯ Low	CRITICAL
Clinical cure rate at 3-4 weeks												
2[1,4]	RCT	Not serious[2]	Not serious	Not serious	Serious[3]	none	152/193 (78.8%)	156/197 (79.2%)	RR 1.01 (0.92 to 1.11)	8 more per 1,000 (from 63 fewer to 87 more)	⨁◯◯◯ Moderate	CRITICAL
Hospital length of stay												
1[1]	RCT	Not serious	Not serious	Not serious	Serious[3]	none	172	171	-	MD 0.35 lower (1.17 lower to 0.47 higher)	⨁◯◯◯ Moderate	IMPORTANT

CI: confidence interval; RR: risk ratio; MD: mean difference.
Footnotes:

1. Dinh, A., Ropers, J., Duran, C., Davido, B., Deconinck, L., Matt, M., Senard, O., Lagrange, A., Makhloufi, S., Mellon, G., de Lastours, V., Bouchand, F., Mathieu, E., Kahn, J. E., Rouveix, E., Grenet, J., Dumoulin, J., Chinet, T., Pépin, M., Delcey, V., Diamantis, S., Benhamou, D., Vitrat, V., Dombret, M. C., Renaud, B., Perronne, C., Claessens, Y. E., Labarère, J., Bedos, J. P., Aegerter, P., Crémieux, A. C.. Discontinuing β-lactam treatment after 3 days for patients with community-acquired pneumonia in non-critical care wards (PTC): a double-blind, randomised, placebo-controlled, non-inferiority trial. Lancet; Mar 27 2021.
2. Risk of bias: Minor protocol violations, judged not severe enough to warrant downgrading.
3. Imprecision: wide confidence intervals, the ends of the confidence interval are likely to lead to different courses of action .
4. el Moussaoui, R., de Borgie, C. A., van den Broek, P., Hustinx, W. N., Bresser, P., van den Berk, G. E., Poley, J. W., van den Berg, B., Krouwels, F. H., Bonten, M. J., Weenink, C., Bossuyt, P. M., Speelman, P., Opmeer, B. C., Prins, J. M.. Effectiveness of discontinuing antibiotic treatment after three days versus eight days in mild to moderate-severe community acquired pneumonia: randomised, double blind study. Bmj; Jun 10 2006.
5. Inconsistency: Significant heterogeneity (defined as p-het <0.05 or I^2 > 50%).

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PICO Question #4: Systemic corticosteroids for CAP

Population: Hospitalized adult CAP patients

Intervention: Corticosteroids

Comparator: No corticosteroids

Outcomes:

Critical

Mortality

Treatment/clinical failure

Clinical stability

Adverse drug events

Important

Symptoms

Disability or return to independence/function

Length of stay

Antibiotic days

Search strategy

admission"[All Fields])) AND ((((("Community-Acquired Infections"[MeSH Terms] OR ("community acquired"[All Fields] AND "infections"[All Fields]) OR "Community-Acquired Infections"[All Fields] OR ("community"[All Fields] AND "acquired"[All Fields] AND "infection"[All Fields]) OR "community acquired infection"[All Fields] OR "Community-Acquired Infections"[MeSH Terms]) AND ("pneumonia"[MeSH Terms] OR "pneumonia"[All Fields] OR "pneumonias"[All Fields] OR "pneumoniae"[All Fields] OR "pneumoniae s"[All Fields])) AND (("respiratory tract infections"[MeSH Terms] OR ("respiratory"[All Fields] AND "tract"[All Fields] AND "infections"[All Fields]) OR "respiratory tract infections"[All Fields]))) AND ((english[Filter]) AND (alladult[Filter])))) AND ((("Adrenal Cortex Hormones"[Mesh])) OR "Steroids/therapeutic use"[Mesh] OR Corticosteroid*) **Filters:** Adult: 19+ years, English **Sort by:** Most Recent

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Figure S7: Flow of information diagram

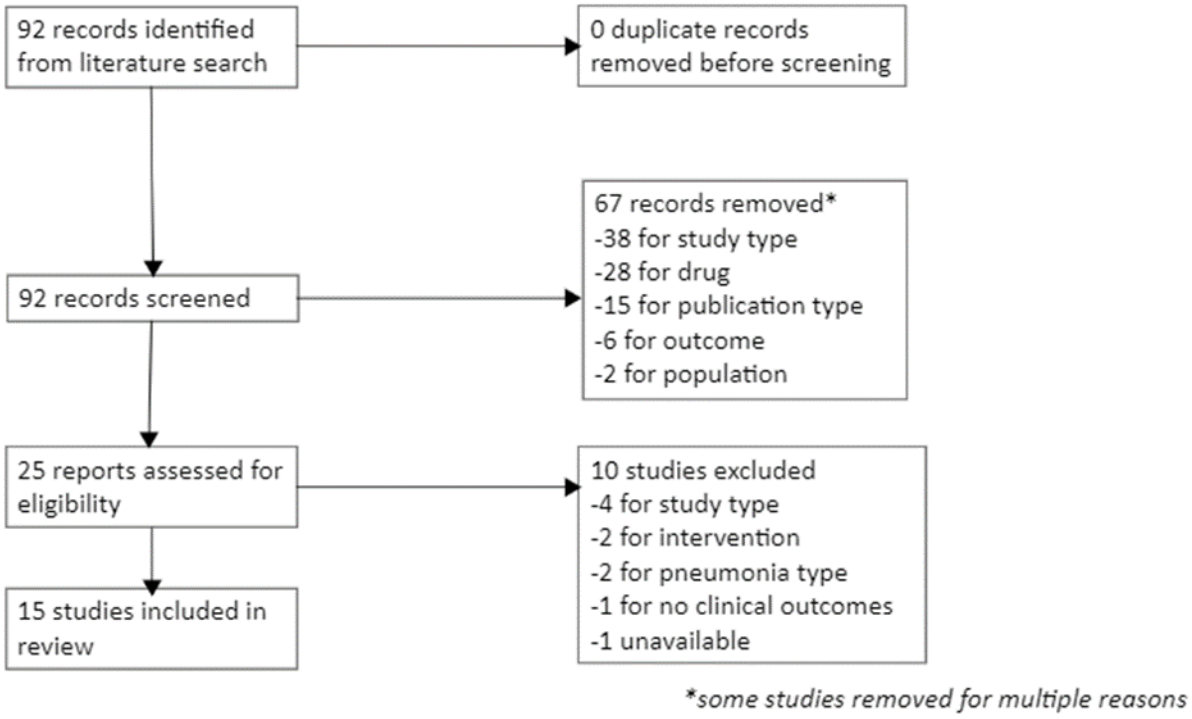

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Table S7: Studies selected

Study	Type of Study	Location	Number of Subjects	Population	Intervention	Outcomes	Risk of Bias
Blum 2015	RCT	Switzerland	785	Hospital admission with CAP[a]	Prednisone 50 mg daily for 7 days	Mortality Clinical stability Adverse drug events Length of stay Antibiotic duration	None
Confalonieri 2005	RCT	Italy	46	ICU admission with severe CAP[b,c]	Hydrocortisone 200 mg IV bolus followed by 10 mg/hour for 7 days	Mortality Adverse drug events Length of stay	Serious
Dequin 2023	RCT	France	800	ICU admission with severe CAP[d]	Hydrocortisone 200 mg per day for 4 days with predefined criteria to administer for a total of 8 or 14 days with gradual taper	Mortality Adverse drug events	Serious
Fernandez 2011	RCT	Spain	45	Hospital admission with CAP[e]	Methylprednisolone 200 mg IV Followed by 20 mg/6 h for 3 days, then 20 mg/12 h for 3 days, then 20 mg/day for 3 days	Mortality Length of stay	Serious
Fitzgerald 2022	RCT	Multinational	79	Hospital admission with CAP and new pleural effusion	Dexamethasone 4 mg IV every 12 hours for 48 hours	Clinical stability Adverse drug events	Very Serious

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						Length of stay Antibiotic duration	
Marik 1993	RCT	South Africa	30	ICU admission with CAP[f]	Hydrocortisone 10 mg/kg	Mortality Length of stay	Very Serious
Meduri 2022	RCT	USA	584	ICU admission with severe CAP[g]	Methylprednisolone 40 mg IV, then 40 mg/day days 1-7, 20 mg/day days 8-14, 12 mg/day days 15-17, and 4 mg/day days 18-20	Mortality Adverse drug events Length of stay	Serious
Meijvis 2011	RCT	Netherlands	304	Hospital admission with CAP[h]	Dexamethasone 5 mg IV followed by 5 mg daily for 3 days	Mortality Length of stay Antibiotic duration	None
Mikami 2007	RCT	Japan	31	Hospital admission with CAP[i]	Prednisolone 40 mg IV daily for 3 days	Length of stay Antibiotic duration	Very Serious
Nafae 2013	RCT	Egypt	80	Hospital admission with CAP[h]	Hydrocortisone 200 mg IV bolus followed by 10 mg/hour for 7 days	Mortality Length of stay Antibiotic duration	Serious
Sabry 2011	RCT	Egypt	80	ICU admission with CAP[g]	Hydrocortisone 200 mg IV bolus followed by 12.5 mg/hour for 7 days	Mortality	Serious
Snijders 2010	RCT	Netherlands	213	Hospital admission with CAP[j]	Prednisone 40 mg daily for 7 days	Mortality Treatment failure Clinical stability	Serious

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						Adverse drug events Length of stay	
Torres 2015	RCT	Spain	120	Hospital admission with severe CAP[c,h]	Methylprednisolone 0.5 mg/kg IV every 12 hours for 5 days	Mortality Treatment failure Clinical stability Length of stay	Serious
Wagner 1956	RCT	USA	113	Hospital admission with confirmed pneumococcal pneumonia	Hydrocortisone PO 80 mg once, then 60 mg every 6 hours for 3 doses, then 40 mg every 6 hours for 4 doses, then 20 mg every 6 hours for 4 doses, then 10 mg every 6 hours for 4 doses, then 10 mg every 12 hours for 2 doses	Mortality	Very Serious
Wittermans 2021	RCT	Netherlands	412	Hospital admission with CAP[k]	Dexamethasone 6 mg PO daily for 4 days	Mortality Length of stay	Serious

[a]Niederman MS, Mandell LA, Anzueto A, et al. Guidelines for the management of adults with community-acquired pneumonia. Diagnosis, assessment of severity, antimicrobial therapy, and prevention. Am J Respir Crit Care Med 2001;163:1730–54.

[b]Niederman MS, Bass JB Jr, Campbell GD, et al. Guidelines for the initial management of adults with community-acquired pneumonia: diagnosis, assessment of severity, and initial antimicrobial therapy. American Thoracic Society. Medical Section of the American Lung Association. Am Rev Respir Dis 1993;148:1418–1426.

[c]Ewig S, Ruiz M, Mensa J, et al. Severe community-acquired pneumonia: assessment of severity criteria. Am J Respir Crit Care Med 1998;158:1102–1108.

[d]Diagnosis of Community-Acquired Pneumonia (CAP) suggested by at least two of the following: cough, purulent sputum, chest pain, dyspnea + Focal shadowing/infiltrate on chest X-ray or CT-scan + one of the following: Pneumonia Severity Index (PSI) > 130 (Fine class V), Patient placed on mechanical ventilation (invasive or not) for acute respiratory failure, with a PEEP level of 5 cm of water or more, Patient treated by high-flow oxygen therapy with a FiO2 of 50% or more and a PaO2:FiO2 ratio lower than 300, or Patient treated by oxygen therapy with a partial rebreathing-mask with a reservoir bag,

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provided that the PaO2 is less than 180 mmHg for oxygen flow 6 L/min, 210 mmHg for oxygen flow 7 L/min, 240 mmHg for 8 L/min, 270 mmHg for 9 L/min, or 300 mHg for 10 L/min or more

[e]Pneumonia based on presence of a lung radiographic opacity and at least two of the following conditions: fever (>38.5°C), purulent expectoration, pleuritic chest pain, or leukocytosis (white blood cell count of >10,000/mm3) + with extensive radiographic consolidations (affecting at least two lobes) and respiratory failure (ratio of partial O2 pressure to the fraction of inspired O2, <300)

[f]British Thoracic Society Research Committee. Community-acquired pneumonia in adults in British Hospitals in 1982-1983: a survey of aetiology, mortality, prognostic factors and outcome. Q J Med 1987;62:195-220

[g]Mandell LA, Wunderink RG, Anzueto A, et al. Infectious diseases society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. 2007;Clin Infect Dis 44(Suppl 2):S27-72

[h]Fine MJ, Singer DE, Hanusa BH, et al. Validation of a pneumonia prognostic index using the MedisGroups Comparative Hospital Database. Am J Med 993;94:153–59.

[l]Clinical signs and symptoms of lower respiratory tract infections + Radiographic abnormalities consistent with infection neither preexisting nor caused by any other previous conditions

[j]Clinical symptoms suggestive of CAP: cough (with or without sputum), fever (.38.58C), pleuritic chest pain, or dyspnea + new consolidations on chest radiograph.

[k]New opacities on chest radiography, and two of the following signs and symptoms: cough, production of sputum, temperature >38.0°C or <36.0°C, abnormalities at auscultation consistent with pneumonia, C-reactive protein (CRP) >15 mg/L, white blood cell count >10×109 or <4×109 cell/L, or >10% of bands in leukocyte differentiation

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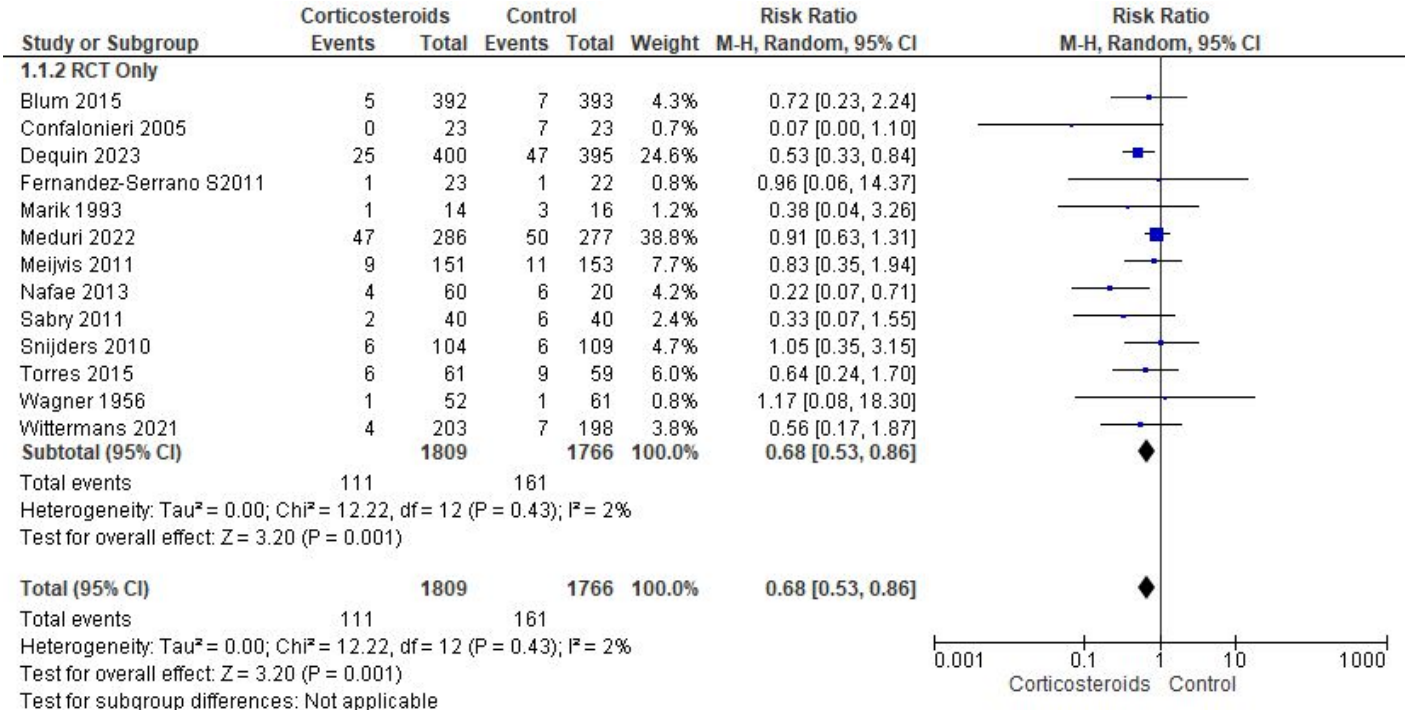
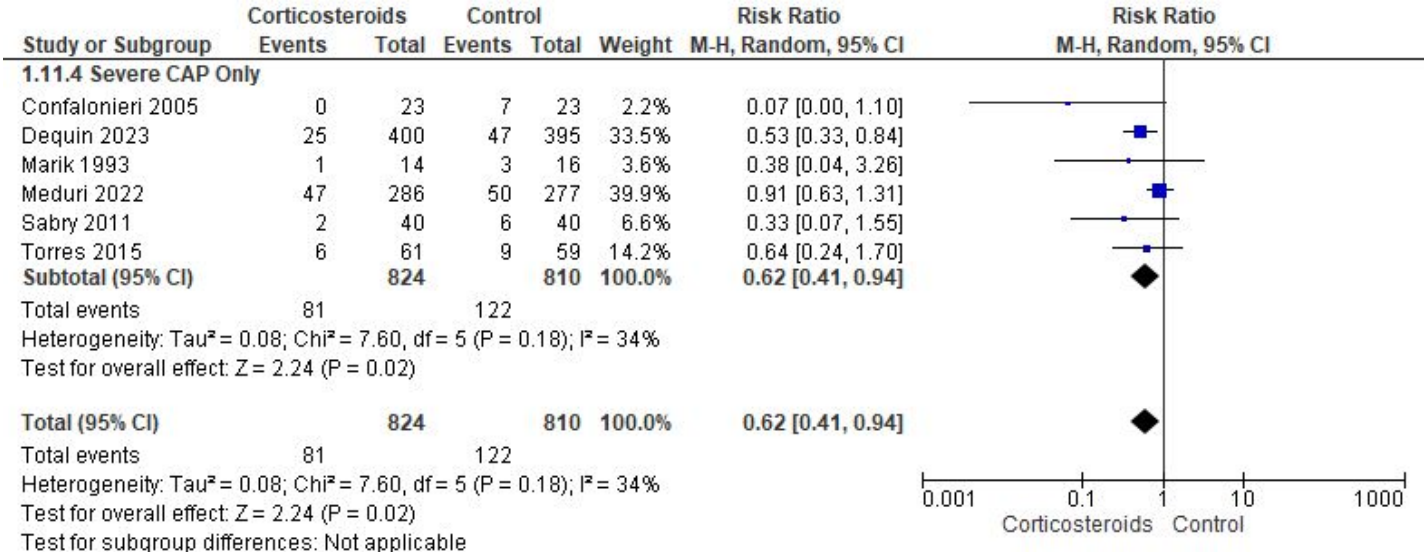
Figure S8: Forest plots

A) Analysis #1: Mortality in CAP



B) Analysis #2: Mortality in Severe CAP



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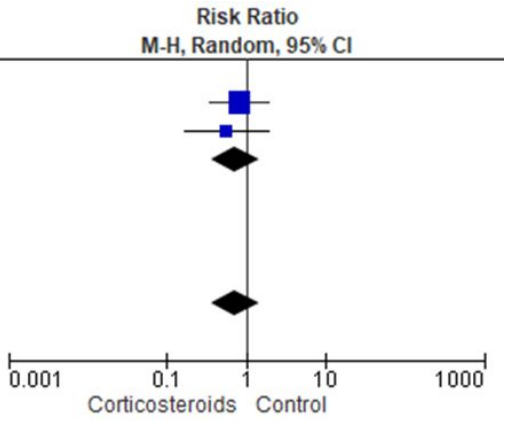
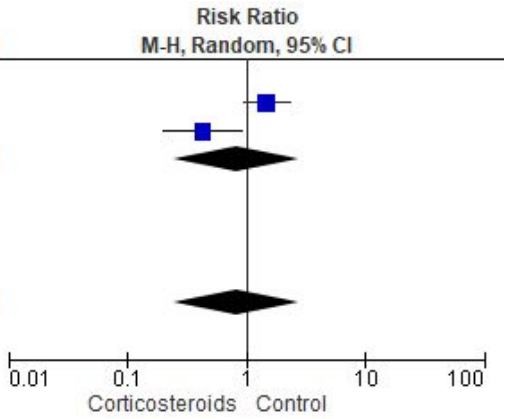
C) Analysis #3: Mortality in CAP Patients Admitted to Ward

Study or Subgroup	Corticosteroids Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.11.5 Ward Patients Only						
Meijvis 2011	9	151	11	153	67.0%	0.83 [0.35, 1.94]
Wittermans 2021	4	203	7	198	33.0%	0.56 [0.17, 1.87]
Subtotal (95% CI)		**354**		**351**	**100.0%**	**0.73 [0.36, 1.46]**
Total events	13		18			
Heterogeneity: Tau² = 0.00; Chi² = 0.28, df = 1 (P = 0.60); I² = 0%						
Test for overall effect: Z = 0.90 (P = 0.37)						
Total (95% CI)		**354**		**351**	**100.0%**	**0.73 [0.36, 1.46]**
Total events	13		18			
Heterogeneity: Tau² = 0.00; Chi² = 0.28, df = 1 (P = 0.60); I² = 0%						
Test for overall effect: Z = 0.90 (P = 0.37)						
Test for subgroup differences: Not applicable						



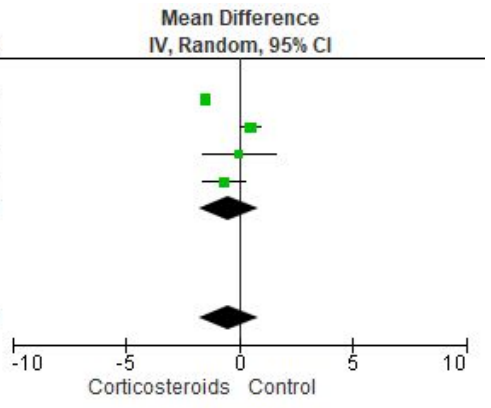
D) Analysis #4: Treatment Failure in CAP

Study or Subgroup	Corticosteroids Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.2.1 RCTs Only						
Snijders 2010	34	104	24	109	53.1%	1.48 [0.95, 2.32]
Torres 2015	8	61	18	59	46.9%	0.43 [0.20, 0.91]
Subtotal (95% CI)		**165**		**168**	**100.0%**	**0.83 [0.25, 2.80]**
Total events	42		42			
Heterogeneity: Tau² = 0.67; Chi² = 7.76, df = 1 (P = 0.005); I² = 87%						
Test for overall effect: Z = 0.30 (P = 0.76)						
Total (95% CI)		**165**		**168**	**100.0%**	**0.83 [0.25, 2.80]**
Total events	42		42			
Heterogeneity: Tau² = 0.67; Chi² = 7.76, df = 1 (P = 0.005); I² = 87%						
Test for overall effect: Z = 0.30 (P = 0.76)						
Test for subgroup differences: Not applicable						



E) Analysis #5: Clinical Stability in CAP

Study or Subgroup	Corticosteroids Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.3.1 RCTs Only								
Blum 2015	2.97	0.67	392	4.47	0.74	393	28.3%	-1.50 [-1.60, -1.40]
Fitzgerald 2022	1.78	0.7	51	1.28	1.11	28	27.4%	0.50 [0.05, 0.95]
Snijders 2010	4.9	6.8	104	4.9	5.2	109	19.7%	0.00 [-1.63, 1.63]
Torres 2015	4.33	2.28	61	5	3.04	59	24.6%	-0.67 [-1.63, 0.29]
Subtotal (95% CI)			**608**			**589**	**100.0%**	**-0.45 [-1.77, 0.86]**
Heterogeneity: Tau² = 1.59; Chi² = 76.31, df = 3 (P < 0.00001); I² = 96%								
Test for overall effect: Z = 0.67 (P = 0.50)								
Total (95% CI)			**608**			**589**	**100.0%**	**-0.45 [-1.77, 0.86]**
Heterogeneity: Tau² = 1.59; Chi² = 76.31, df = 3 (P < 0.00001); I² = 96%								
Test for overall effect: Z = 0.67 (P = 0.50)								
Test for subgroup differences: Not applicable								



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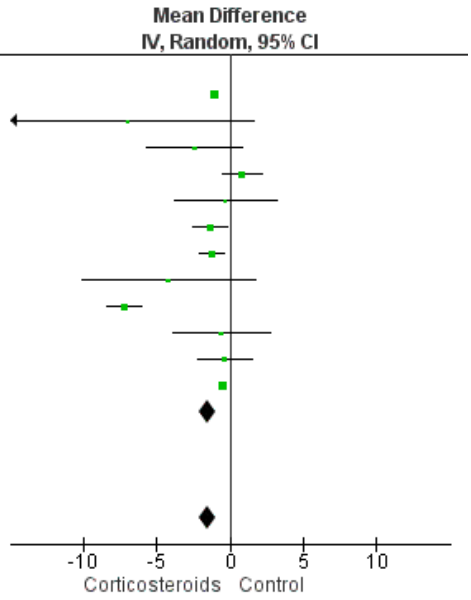
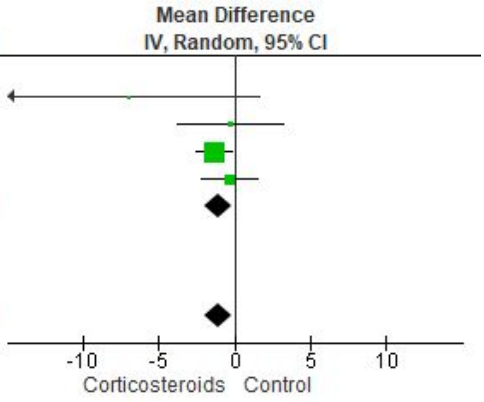
F) Analysis #6: Length of Stay in CAP

Study or Subgroup	Corticosteroids Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.11.2 RCTs Only								
Blum 2015	6.33	0.74	392	7.33	0.74	393	18.7%	-1.00 [-1.10, -0.90]
Confalonieri 2005	22.25	11.15	23	29.25	17.89	23	0.5%	-7.00 [-15.62, 1.62]
Fernandez-Serrano S2011	10.6	3.16	23	13	7.13	22	3.0%	-2.40 [-5.65, 0.85]
Fitzgerald 2022	7	3.81	51	6.17	2.34	28	9.8%	0.83 [-0.53, 2.19]
Marik 1993	4.3	3.8	14	4.6	5.9	16	2.6%	-0.30 [-3.81, 3.21]
Meduri 2022	7.67	5.96	297	9	8.2	287	11.2%	-1.33 [-2.50, -0.16]
Meijvis 2011	6.83	2.99	151	8.07	4.71	153	13.5%	-1.24 [-2.13, -0.35]
Mikami 2007	11.3	5.5	15	15.5	10.7	16	1.0%	-4.20 [-10.14, 1.74]
Nafae 2013	9.27	2.4	60	16.5	2.24	20	11.3%	-7.23 [-8.38, -6.08]
Snijders 2010	10	12	104	10.6	12.8	109	2.9%	-0.60 [-3.93, 2.73]
Torres 2015	10.83	4.94	61	11.17	5.32	59	7.0%	-0.34 [-2.18, 1.50]
Wittermans 2021	4.5	0.75	203	5	0.6	198	18.6%	-0.50 [-0.63, -0.37]
Subtotal (95% CI)			**1394**			**1324**	**100.0%**	**-1.53 [-2.14, -0.91]**
Heterogeneity: Tau² = 0.52; Chi² = 163.82, df = 11 (P < 0.00001); I² = 93%								
Test for overall effect: Z = 4.89 (P < 0.00001)								
Total (95% CI)			**1394**			**1324**	**100.0%**	**-1.53 [-2.14, -0.91]**
Heterogeneity: Tau² = 0.52; Chi² = 163.82, df = 11 (P < 0.00001); I² = 93%								
Test for overall effect: Z = 4.89 (P < 0.00001)								
Test for subgroup differences: Not applicable								



G) Analysis #7: Length of Stay in Severe CAP

Study or Subgroup	Corticosteroids Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.2.3 Severe CAP								
Confalonieri 2005	22.25	11.15	23	29.25	17.89	23	1.2%	-7.00 [-15.62, 1.62]
Marik 1993	4.3	3.8	14	4.6	5.9	16	7.2%	-0.30 [-3.81, 3.21]
Meduri 2022	7.67	5.96	297	9	8.2	287	65.3%	-1.33 [-2.50, -0.16]
Torres 2015	10.83	4.94	61	11.17	5.32	59	26.3%	-0.34 [-2.18, 1.50]
Subtotal (95% CI)			**395**			**385**	**100.0%**	**-1.06 [-2.01, -0.12]**
Heterogeneity: Tau² = 0.00; Chi² = 2.80, df = 3 (P = 0.42); I² = 0%								
Test for overall effect: Z = 2.21 (P = 0.03)								
Total (95% CI)			**395**			**385**	**100.0%**	**-1.06 [-2.01, -0.12]**
Heterogeneity: Tau² = 0.00; Chi² = 2.80, df = 3 (P = 0.42); I² = 0%								
Test for overall effect: Z = 2.21 (P = 0.03)								
Test for subgroup differences: Not applicable								



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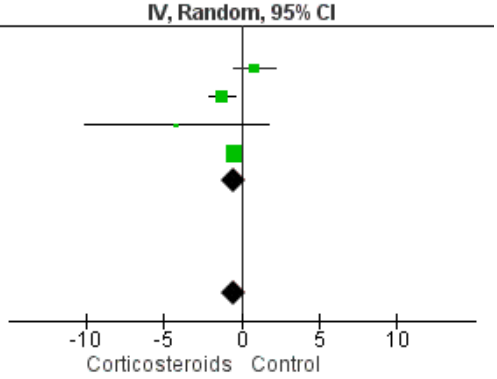
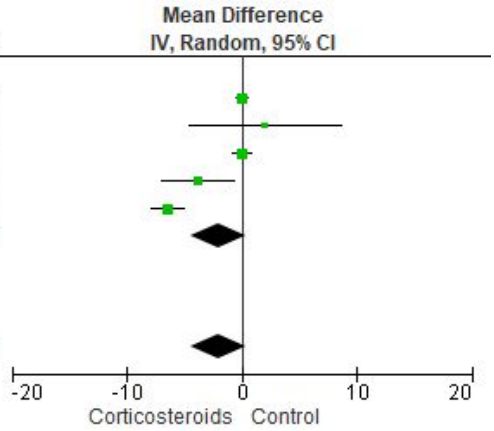
H) Analysis #8: Length of Stay in CAP Patients Admitted to Ward

Study or Subgroup	Corticosteroids Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.12.4 Ward Patients Only								
Fitzgerald 2022	7	3.81	51	6.17	2.34	28	20.3%	0.83 [-0.53, 2.19]
Meijvis 2011	6.83	2.99	151	8.07	4.71	153	30.4%	-1.24 [-2.13, -0.35]
Mikami 2007	11.3	5.5	15	15.5	10.7	16	1.8%	-4.20 [-10.14, 1.74]
Wittermans 2021	4.5	0.75	203	5	0.6	198	47.5%	-0.50 [-0.63, -0.37]
Subtotal (95% CI)			**420**			**395**	**100.0%**	**-0.52 [-1.33, 0.28]**
Heterogeneity: Tau² = 0.35; Chi² = 7.85, df = 3 (P = 0.05); I² = 62%								
Test for overall effect: Z = 1.27 (P = 0.21)								
Total (95% CI)			**420**			**395**	**100.0%**	**-0.52 [-1.33, 0.28]**
Heterogeneity: Tau² = 0.35; Chi² = 7.85, df = 3 (P = 0.05); I² = 62%								
Test for overall effect: Z = 1.27 (P = 0.21)								
Test for subgroup differences: Not applicable								



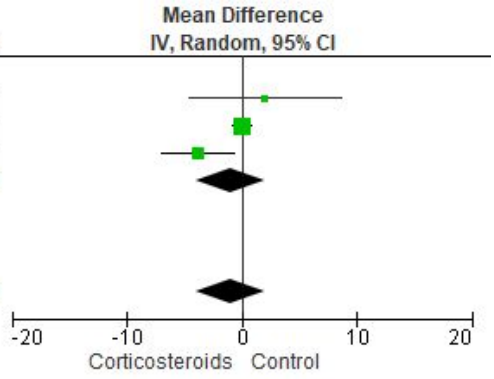
I) Analysis #9: Antibiotic Duration in CAP

Study or Subgroup	Corticosteroids Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.1.1 RCTs Only								
Blum 2015	9	2.97	392	9	3.72	393	25.2%	0.00 [-0.47, 0.47]
Fitzgerald 2022	22.4	15.4	51	20.4	13.8	28	8.9%	2.00 [-4.63, 8.63]
Meijvis 2011	5	4.2	151	5	3.5	153	24.6%	0.00 [-0.87, 0.87]
Mikami 2007	8.5	3.2	15	12.3	5.5	16	17.9%	-3.80 [-6.94, -0.66]
Nafae 2013	7.45	2.6	60	13.9	2.98	20	23.3%	-6.45 [-7.91, -4.99]
Subtotal (95% CI)			**669**			**610**	**100.0%**	**-2.01 [-4.46, 0.45]**
Heterogeneity: Tau² = 6.17; Chi² = 73.96, df = 4 (P < 0.00001); I² = 95%								
Test for overall effect: Z = 1.60 (P = 0.11)								
Total (95% CI)			**669**			**610**	**100.0%**	**-2.01 [-4.46, 0.45]**
Heterogeneity: Tau² = 6.17; Chi² = 73.96, df = 4 (P < 0.00001); I² = 95%								
Test for overall effect: Z = 1.60 (P = 0.11)								
Test for subgroup differences: Not applicable								



J) Analysis #10: Antibiotic Duration in CAP Patients Admitted to Ward

Study or Subgroup	Corticosteroids Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.5.2 Ward Patients Only								
Fitzgerald 2022	22.4	15.4	51	20.4	13.8	28	14.5%	2.00 [-4.63, 8.63]
Meijvis 2011	5	4.2	151	5	3.5	153	52.0%	0.00 [-0.87, 0.87]
Mikami 2007	8.5	3.2	15	12.3	5.5	16	33.6%	-3.80 [-6.94, -0.66]
Subtotal (95% CI)			**217**			**197**	**100.0%**	**-0.99 [-3.93, 1.96]**
Heterogeneity: Tau² = 4.14; Chi² = 5.66, df = 2 (P = 0.06); I² = 65%								
Test for overall effect: Z = 0.66 (P = 0.51)								
Total (95% CI)			**217**			**197**	**100.0%**	**-0.99 [-3.93, 1.96]**
Heterogeneity: Tau² = 4.14; Chi² = 5.66, df = 2 (P = 0.06); I² = 65%								
Test for overall effect: Z = 0.66 (P = 0.51)								
Test for subgroup differences: Not applicable								



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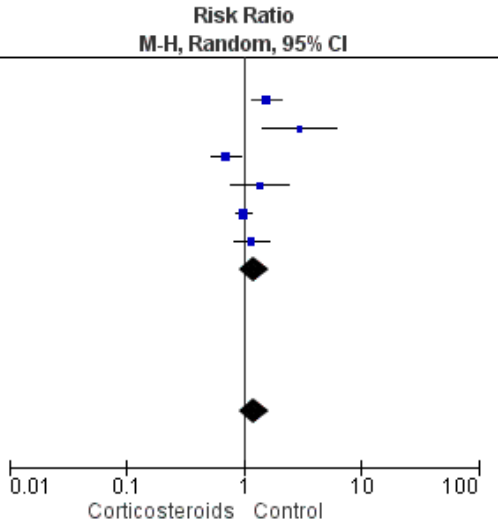
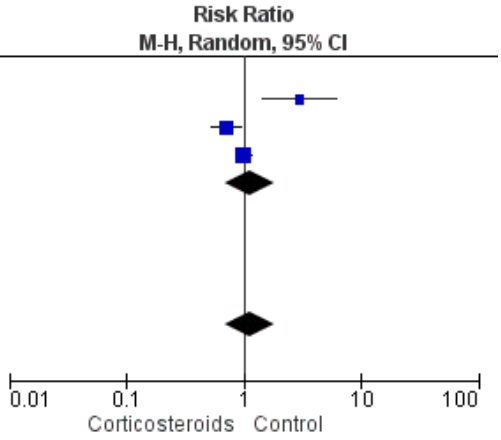
K) Analysis #11: Adverse Events in CAP

Study or Subgroup	Corticosteroids Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.6.1 RCTs Only						
Blum 2015	96	392	61	393	19.1%	1.58 [1.18, 2.11]
Confalonieri 2005	18	23	6	23	9.7%	3.00 [1.46, 6.17]
Dequin 2023	63	400	88	395	19.0%	0.71 [0.53, 0.95]
Fitzgerald 2022	25	51	10	28	12.4%	1.37 [0.78, 2.43]
Meduri 2022	167	297	162	287	22.2%	1.00 [0.86, 1.15]
Snijders 2010	41	104	37	109	17.5%	1.16 [0.82, 1.65]
Subtotal (95% CI)		**1267**		**1235**	**100.0%**	**1.21 [0.90, 1.62]**
Total events	410		364			
Heterogeneity: Tau² = 0.10; Chi² = 24.53, df = 5 (P = 0.0002); I² = 80%						
Test for overall effect: Z = 1.29 (P = 0.20)						
Total (95% CI)		**1267**		**1235**	**100.0%**	**1.21 [0.90, 1.62]**
Total events	410		364			
Heterogeneity: Tau² = 0.10; Chi² = 24.53, df = 5 (P = 0.0002); I² = 80%						
Test for overall effect: Z = 1.29 (P = 0.20)						
Test for subgroup differences: Not applicable						



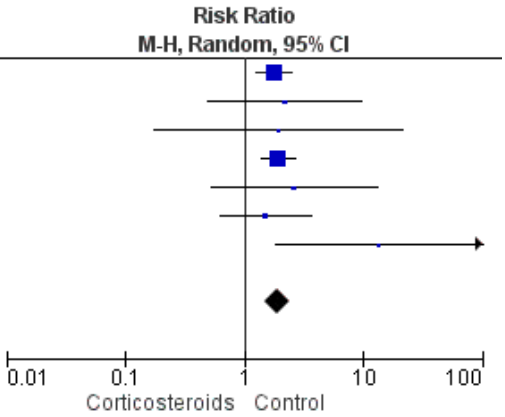
L) Analysis #12: Adverse Events in Severe CAP

Study or Subgroup	Corticosteroids Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.13.2 Severe CAP						
Confalonieri 2005	18	23	6	23	22.0%	3.00 [1.46, 6.17]
Dequin 2023	63	400	88	395	36.9%	0.71 [0.53, 0.95]
Meduri 2022	167	297	162	287	41.1%	1.00 [0.86, 1.15]
Subtotal (95% CI)		**720**		**705**	**100.0%**	**1.12 [0.69, 1.82]**
Total events	248		256			
Heterogeneity: Tau² = 0.14; Chi² = 14.20, df = 2 (P = 0.0008); I² = 86%						
Test for overall effect: Z = 0.45 (P = 0.65)						
Total (95% CI)		**720**		**705**	**100.0%**	**1.12 [0.69, 1.82]**
Total events	248		256			
Heterogeneity: Tau² = 0.14; Chi² = 14.20, df = 2 (P = 0.0008); I² = 86%						
Test for overall effect: Z = 0.45 (P = 0.65)						
Test for subgroup differences: Not applicable						



M) Analysis #13: Hyperglycemia in CAP

Study or Subgroup	Corticosteroids Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Blum 2015	76	392	43	393	42.7%	1.77 [1.25, 2.51]
Fitzgerald 2022	8	51	2	28	2.3%	2.20 [0.50, 9.64]
Meduri 2022	2	297	1	287	0.9%	1.93 [0.18, 21.20]
Meijvis 2011	67	151	35	153	44.1%	1.94 [1.38, 2.73]
Snijders 2010	5	104	2	109	2.0%	2.62 [0.52, 13.21]
Torres 2015	11	61	7	59	6.7%	1.52 [0.63, 3.66]
Wittermans 2021	14	203	1	198	1.3%	13.66 [1.81, 102.86]
Total (95% CI)		**1259**		**1227**	**100.0%**	**1.90 [1.51, 2.38]**
Total events	183		91			
Heterogeneity: Tau² = 0.00; Chi² = 4.40, df = 6 (P = 0.62); I² = 0%						
Test for overall effect: Z = 5.54 (P < 0.00001)						



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N) Analysis #14: Gastrointestinal Bleeding in CAP

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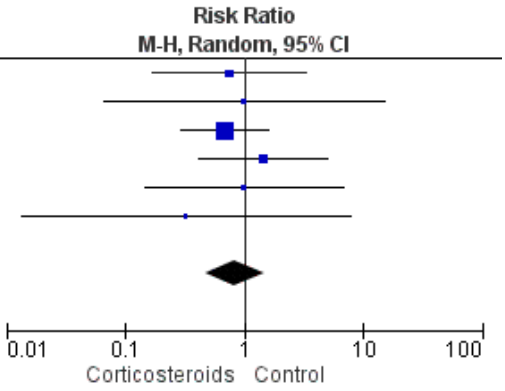
Study or Subgroup	Corticosteroids Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Blum 2015	3	392	4	393	14.9%	0.75 [0.17, 3.34]
Confalonieri 2005	1	23	1	23	4.5%	1.00 [0.07, 15.04]
Dequin 2023	9	400	13	395	47.2%	0.68 [0.30, 1.58]
Meduri 2022	6	297	4	287	21.1%	1.45 [0.41, 5.08]
Sabry 2011	2	40	2	40	9.1%	1.00 [0.15, 6.76]
Torres 2015	0	61	1	59	3.3%	0.32 [0.01, 7.76]
Total (95% CI)		**1213**		**1197**	**100.0%**	**0.83 [0.47, 1.48]**
Total events	21		25			

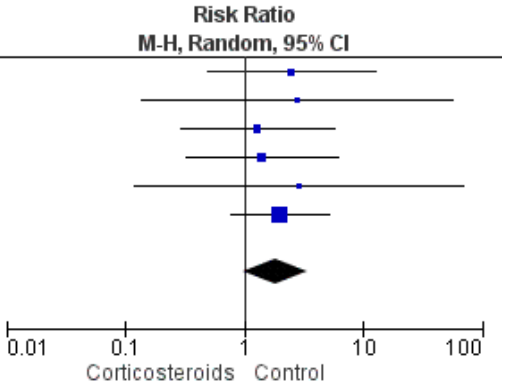
Heterogeneity: Tau² = 0.00; Chi² = 1.37, df = 5 (P = 0.93); I² = 0%
Test for overall effect: Z = 0.62 (P = 0.54)



O) Analysis #15: Neuropsychiatric Events in CAP

Study or Subgroup	Corticosteroids Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Blum 2015	5	392	2	393	14.4%	2.51 [0.49, 12.84]
Fitzgerald 2022	2	51	0	28	4.3%	2.79 [0.14, 56.13]
Meduri 2022	4	297	3	287	17.3%	1.29 [0.29, 5.71]
Snijders 2010	4	104	3	109	17.7%	1.40 [0.32, 6.09]
Torres 2015	1	61	0	59	3.8%	2.90 [0.12, 69.87]
Wittermans 2021	10	209	7	293	42.6%	2.00 [0.77, 5.18]
Total (95% CI)		**1114**		**1169**	**100.0%**	**1.85 [1.00, 3.44]**
Total events	26		15			

Heterogeneity: Tau² = 0.00; Chi² = 0.68, df = 5 (P = 0.98); I² = 0%
Test for overall effect: Z = 1.95 (P = 0.05)



P) Analysis #16: Nosocomial Infection in CAP

Study or Subgroup	Corticosteroids Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Blum 2015	13	392	14	393	11.3%	0.93 [0.44, 1.95]
Confalonieri 2005	0	23	4	23	0.8%	0.11 [0.01, 1.95]
Dequin 2023	39	400	44	395	31.4%	0.88 [0.58, 1.32]
Fitzgerald 2022	2	51	3	28	2.2%	0.37 [0.06, 2.06]
Meduri 2022	59	297	56	287	43.4%	1.02 [0.73, 1.41]
Meijvis 2011	7	151	5	153	5.1%	1.42 [0.46, 4.37]
Snijders 2010	10	104	4	109	5.1%	2.62 [0.85, 8.09]
Torres 2015	1	61	0	59	0.7%	2.90 [0.12, 69.87]
Total (95% CI)		**1479**		**1447**	**100.0%**	**0.99 [0.76, 1.29]**
Total events	131		130			

Heterogeneity: Tau² = 0.01; Chi² = 7.61, df = 7 (P = 0.37); I² = 8%
Test for overall effect: Z = 0.06 (P = 0.95)

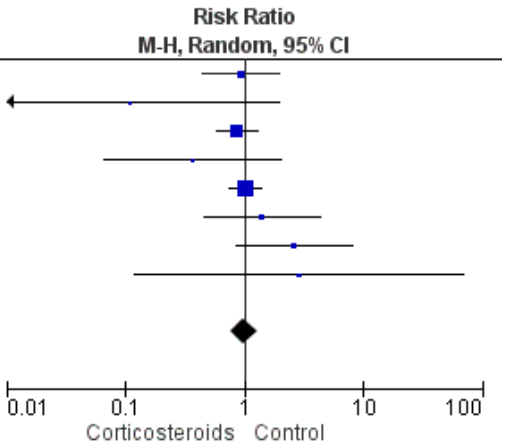


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Table S8: Evidence profiles

Table S8.1
Population: Adults with CAP
Comparison: Systemic corticosteroids versus no systemic corticosteroids
Setting: All patients (outpatients and inpatients)

Quality assessment							Summary of Findings				Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Steroids	Placebo	Relative Effect (95% CI)	Absolute Effect (95% CI)		
Mortality												
13[1-13]	RCT	Serious[14]	Not serious	Not serious	Not serious	None	111/1809 (6.1%)	161/1766 (9.1%)	RR 0.68 (0.53 to 0.86)	29.12 per 1000 (42.77 to 12.74)	⊕◯◯◯ Moderate	CRITICAL
Treatment Failure												
2[10-11]	RCT	Not serious	Serious[15]	Not serious	Serious[16]	None	42/165 (25.5%)	42/168 (25.0%)	RR 0.83 (0.25 to 2.80)	52.53 per 1000 (231.75 to - 556.20)	⊕⊕◯◯ Low	CRITICAL
Clinical Stability												
4[1,10-11,17]	RCT	Serious[14]	Serious[15]	Not serious[18]	Serious[16]	None	682	654	-	MD -0.45 (-1.77 to 0.86)	⊕◯◯◯ Very Low	CRITICAL
Adverse Events												
6[1,2-3,6,10,17]	RCT	Not serious	Serious[15]	Not serious[18]	Serious[16]	None	410/1267 (32.4%)	364/1235 (29.5%)	RR 1.21 (0.90 to 1.62)	-61.95 per 1000 (29.5 to - 182.9)	⊕⊕◯◯ Low	CRITICAL
Length of Stay												
12[1,2,4-8,10-11,13,17-15]	RCT	Serious[14]	Serious[15]	Not serious[18]	Not serious	None	1394	1324	-	MD -1.53 (-2.14 to - 0.91)	⊕⊕◯◯ Low	IMPORTANT
Antibiotic Duration												
5[1,7-8,17-19]	RCT	Not serious	Serious[15]	Serious[18,20]	Serious[16]	None	669	610	-	MD -2.01 (-4.46 to 0.45)	⊕◯◯◯ Very Low	IMPORTANT

CI: confidence interval; RCT: randomized controlled trial; RR: risk ratio; MD: mean difference.
Footnotes:

[1] Blum CA, Nigro N, Briel M, et al. Adjunct prednisone therapy for patients with community-acquired pneumonia: a multicentre, double-blind, randomised, placebo-controlled trial. Lancet. 2015;385(9977):1511-8. doi: 10.1016/S0140-6736(14)62447-8.
[2] Confalonieri M, Urbino R, Potena A, et al Hydrocortisone infusion for severe community-acquired pneumonia: a preliminary randomized study. Am J Respir Crit Care Med. 2005;171(3):242-8. doi: 10.1164/rccm.200406-808OC. Epub 2004 Nov 19. PMID: 15557131.
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[5] Marik P, Kraus P, Sribante J, Havlik I, Lipman J, Johnson DW. Hydrocortisone and tumor necrosis factor in severe community-acquired pneumonia. A randomized controlled study. Chest. 1993;104(2):389-92. doi: 10.1378/chest.104.2.389.
[6] Meduri GU, Shih MC, Bridges L, et al. Low-dose methylprednisolone treatment in critically ill patients with severe community-acquired pneumonia. Intensive Care Med. 2022;48(8):1009-1023. doi: 10.1007/s00134-022-06684-3.
[7] Meijvis SC, Hardeman H, Remmelts HH, et al. Dexamethasone and length of hospital stay in patients with community-acquired pneumonia: a randomised, double-blind, placebo-controlled trial. Lancet. 2011;377(9782):2023-30. doi: 10.1016/S0140-6736(11)60607-7.
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[10] Snijders D, Daniels JM, de Graaff CS, van der Werf TS, Boersma WG. Efficacy of corticosteroids in community-acquired pneumonia: a randomized double-blinded clinical trial. Am J Respir Crit Care Med. 2010;181(9):975-82. doi: 10.1164/rccm.200905-0808OC.
[11] Torres A, Sibila O, Ferrer M, Polverino E, et al. Effect of corticosteroids on treatment failure among hospitalized patients with severe community-acquired pneumonia and high inflammatory response: a randomized clinical trial. JAMA. 2015;313(7):677-86. doi: 10.1001/jama.2015.88.
[12] Wagner HN Jr, Bennett IL Jr, Lasagna L, Cluff LE, Rosenthal MB, Mirick GS. The effect of hydrocortisone upon the course of pneumococcal pneumonia treated with penicillin. Bull Johns Hopkins Hosp. 1956;98(3):197-215.
[13] Wittermans E, Vestjens SMT, Spoorenberg SMC, et al. Adjunctive treatment with oral dexamethasone in non-ICU patients hospitalised with community-acquired pneumonia: a randomised clinical trial. Eur Respir J. 2021;58(2):2002535. doi: 10.1183/13993003.02535-2020.
[14] Risk of bias: Several studies have either an unclear risk of bias or a high risk of bias due to outcome reported differing from protocol, protocol violations, early study termination, limited information regarding randomization or enrollment procedures, etc.
[15] Inconsistency: Large heterogeneity ($p<0.05$ or $I^2>50\%$)
[16] Imprecision: Wide confidence intervals, defined as the ends of the confidence intervals leading to different courses of action.
[17] Fitzgerald DB, Waterer GW, Budgeon C, et al. Steroid Therapy and Outcome of Parapneumonic Pleural Effusions (STOPPE): A Pilot Randomized Clinical Trial. Am J Respir Crit Care Med. 2022;205(9):1093-1101. doi: 10.1164/rccm.202107-1600OC.
[18] Indirectness of the population: Fitzgerald enrolled patients with a pleural effusion who received antibiotics for a longer duration; therefore, it is likely that the population was more severely ill. However. The committee concluded that this did not alter its confidence in the estimated effects because it was only one of many studies.
[19] Mikami K, Suzuki M, Kitagawa H, et al. Efficacy of corticosteroids in the treatment of community-acquired pneumonia requiring hospitalization. Lung. 2007;185(5):249-255. doi: 10.1007/s00408-007-9020-3.
[20] Indirectness of outcomes: Varied definition of outcomes between studies.

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Table S8.2
Population: Adult inpatients with severe CAP
Comparison: Systemic corticosteroids versus no systemic corticosteroids
Setting: Intensive care units

Quality assessment							Summary of Findings				Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Steroids	Placebo	Relative Effect (95% CI)	Absolute Effect (95% CI)		
Mortality												
6[1-6]	RCT	Serious[7]	Not serious	Not serious[8]	Not serious	None	81/824 (9.8%)	122/810 (15.1%)	RR 0.62 (0.41 to 0.94)	57.38 per 1000 (89.09 to 9.06)	⊕◯◯◯ Moderate	CRITICAL
Adverse Events												
3[1-2,5]	RCT	Not serious	Serious[9]	Not serious[8]	Serious[10]	None	248/720 (34.4%)	256/705 (36.3%)	RR 1.12 (0.69 to 1.82)	43.56 per 1000 (112.53 to -298.66)	⊕⊕◯◯ Low	CRITICAL
Length of Stay												
4[1,3,5,6]	RCT	Serious[7]	Not serious	Not serious[8]	Not serious	None	395	385	-	MD -1.06 (-2.01 to -0.12)	⊕⊕◯◯ Low	IMPORTANT

CI: confidence interval. CO: cohort study. MD: mean difference. OBS: RCT: randomized controlled trial. RR: risk ratio.
Footnotes:
[1] Confalonieri M, Urbino R, Potena A, et al Hydrocortisone infusion for severe community-acquired pneumonia: a preliminary randomized study. Am J Respir Crit Care Med. 2005;171(3):242-8. doi: 10.1164/rccm.200406-808OC. Epub 2004 Nov 19. PMID: 15557131.
[2] Dequin PF, Meziani F, Quenot JP, et al. Hydrocortisone in Severe Community-Acquired Pneumonia. N Engl J Med. 2023. doi: 10.1056/NEJMoa2215145. Epub ahead of print. PMID: 36942789.
[3] Marik P, Kraus P, Sribante J, Havlik I, Lipman J, Johnson DW. Hydrocortisone and tumor necrosis factor in severe community-acquired pneumonia. A randomized controlled study. Chest. 1993;104(2):389-92. doi: 10.1378/chest.104.2.389.
[4] Sabry N, Omar E. Corticosteroids and ICU Course of Community Acquired Pneumonia in Egyptian Settings. Pharmacology & Pharmacy. 2011;2(2):73-81. doi: 10.4236/pp.2011.22009.
[5] Meduri GU, Shih MC, Bridges L, et al. Low-dose methylprednisolone treatment in critically ill patients with severe community-acquired pneumonia. Intensive Care Med. 2022;48(8):1009-1023. doi: 10.1007/s00134-022-06684-3.
[6] Torres A, Sibila O, Ferrer M, Polverino E, et al. Effect of corticosteroids on treatment failure among hospitalized patients with severe community-acquired pneumonia and high inflammatory response: a randomized clinical trial. JAMA. 2015;313(7):677-86. doi: 10.1001/jama.2015.88.
[7] Risk of bias: Several studies have either an unclear risk of bias or a high risk of bias due to outcome reported differing from protocol, protocol violations, early study termination, limited information regarding randomization or enrollment procedures, etc.
[8] Indirectness: Meduri et al. and Torres et al. included a minority of patients who may have had non-severe CAP. However, the committee concluded that this did not alter its confidence in the estimated effects.
[9] Inconsistency: Large heterogeneity ($p<0.05$, $I2 >50\%$)
[10] Imprecision: Wide confidence intervals, defined as the ends of the confidence intervals leading to different courses of action.

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Table S8.3
Population: Adult inpatients with non-severe CAP
Comparison: Systemic corticosteroids versus no systemic corticosteroids
Setting: Medical wards

Quality assessment							Summary of Findings				Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Steroids	Placebo	Relative Effect (95% CI)	Absolute Effect (95% CI)		
Mortality												
2[1-2]	RCT	Serious[3]	Not serious	Not serious[4]	Serious[5]	None	13/354 (3.7%)	18/351 (5.1%)	RR 0.73 (0.36 to 1.461)	13.77 per 1000 (32.64 to -23.46)	⊕⊕◯◯ Low	CRITICAL
Length of Stay												
4[1-2,6-7]	RCT	Serious[3]	Not serious	Not serious[4]	Serious[5]	None	420	395	-	MD -0.52 (-1.33 to 0.28)	⊕⊕◯◯ Low	IMPORTANT
Antibiotic Duration												
3[1,6-7]	RCT	Not serious	Not serious	Serious[4,8]	Serious[5]	None	217	197	-	MD -0.99 (-3.93 to 1.96)	⊕⊕◯◯ Low	IMPORTANT

CI: confidence interval. CO: cohort study. MD: mean difference. OBS: RCT: randomized controlled trial. RR: risk ratio.
Footnotes:
[1] Meijvis SC, Hardeman H, Remmelts HH, et al. Dexamethasone and length of hospital stay in patients with community-acquired pneumonia: a randomised, double-blind, placebo-controlled trial. Lancet. 2011;377(9782):2023-30. doi: 10.1016/S0140-6736(11)60607-7.
[2] Wittermans E, Vestjens SMT, Spoorenberg SMC, et al. Adjunctive treatment with oral dexamethasone in non-ICU patients hospitalised with community-acquired pneumonia: a randomised clinical trial. Eur Respir J. 2021;58(2):2002535. doi: 10.1183/13993003.02535-2020.
[3] Risk of bias: Several studies have either an unclear risk of bias or a high risk of bias due to outcome reported differing from protocol, protocol violations, early study termination, limited information regarding randomization or enrollment procedures, etc.
[4] Indirectness of the population: Fitzgerald enrolled patients with a pleural effusion who received antibiotics for a longer duration; therefore, it is likely that the population was more severely ill. Meijvis et al. and Wittermans et al. included a minority of patients who may have had non-severe CAP. However, the committee concluded that this did not alter its confidence in the estimated effects because it was only one of many studies.
[5] Imprecision: Wide confidence intervals, defined as the ends of the confidence intervals leading to different courses of action.
[6] Fitzgerald DB, Waterer GW, Budgeon C, et al. Steroid Therapy and Outcome of Parapneumonic Pleural Effusions (STOPPE): A Pilot Randomized Clinical Trial. Am J Respir Crit Care Med. 2022;205(9):1093-1101. doi: 10.1164/rccm.202107-1600OC.
[7] Mikami K, Suzuki M, Kitagawa H, et al. Efficacy of corticosteroids in the treatment of community-acquired pneumonia requiring hospitalization. Lung. 2007;185(5):249-255. doi: 10.1007/s00408-007-9020-3.

[8] Indirectness of outcomes: Varied definition of outcomes between studies.

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Table S9: EtD frameworks

A) Analysis #1: Patients with Severe CAP

QUESTION

Should hospitalized patients with severe community-acquired pneumonia receive systemic corticosteroids rather than no systemic corticosteroids?	
POPULATION:	Hospitalized patients with **SEVERE** community-acquired pneumonia
INTERVENTION:	Systemic corticosteroids
COMPARISON:	No systemic corticosteroids
SETTING:	Inpatients

ASSESSMENT

Desirable Effects
How substantial are the desirable effects? "Substantial" refers to both the importance of the outcomes and the magnitude of effect. As an example, a small improvement in a critical outcome might be more substantial than a large improvement in an unimportant outcome.

JUDGEMENT	**RESEARCH EVIDENCE**
○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know The magnitude of the effect is small but mortality is a very important outcome to most patients. Beneficial effects are seen in heterogeneous populations of patients with CAP. These effects appear to be driven by	DESIRABLE EFFECTS <u>Decreased mortality:</u> CAP patients- 13 RCTs, 3575 patients, 6.1% versus 9.1% (NNT 34), RR 0.68, 95% CI 0.53-0.86. Severe CAP- 6 RCTs, 1634 patients, 9.8% versus 15.1% (NNT 17), RR 0.62, 95% CI 0.41-0.94. Non-severe CAP- 3 RCTs, 705 patients, 3.7% versus 5.1% (NNT 72) RR 0.73, 95% CI 0.36 to 1.46. <u>Decreased length of stay:</u> CAP patients- 12 RCTs, 3403 patients, MD -1.11 days, 95% CI -1.66 to -0.55 days. Severe CAP- 4 RCTs, 780 patients, MD -1.06 days, 95% CI -2.01 to -0.12 days. Non-severe CAP – 5 RCTs, 1556 patients, MD -0.61 days, 95% CI -1.36 to 0.14 days. RCT= randomized controlled trial, NNT= number needed to treat, RR = risk ratio, CI = confidence interval, MD = mean difference.

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patients with severe CAP.	

Undesirable Effects How substantial are the undesirable effects? "Substantial" refers to both the importance of the outcomes and the magnitude of effect. As an example, a small increase in a critical adverse outcome might be more substantial than a large increase in an unimportant adverse outcome.	
JUDGEMENT	**RESEARCH EVIDENCE**
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know The magnitude of the effect is small and is of average importance since it is treatable and reversible upon discontinuation.	UNDESIRABLE EFFECTS <u>Increased hyperglycemia:</u> CAP patients- 7 RCTs, 2476 patients, 14.5% versus 9% (NNH 18), RR 1.71, 95% 1.21-2.40. Severe CAP- no research evidence. Non-severe CAP- no research evidence. RCT= randomized controlled trial, NNH = number needed to harm, RR = risk ratio, CI = confidence interval.

Certainty of evidence What is the committee's confidence in the accuracy of the above listed estimates (i.e., what is the quality of evidence)?	
JUDGEMENT	**RESEARCH EVIDENCE**
○ Very low ● Low ○ Moderate ○ High ○ No included studies	QUALITY OF EVIDENCE Overall quality of evidence is the lowest quality of evidence among the critical outcomes. For the critical outcome of <u>adverse effects</u>, there is low-quality evidence because there are RCTs downgraded for inconsistency and imprecision.

Balance of effects Does the balance between desirable and undesirable effects favor the intervention or the comparison?	
JUDGEMENT	**RESEARCH EVIDENCE**

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○ Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ● Favors the intervention ○ Varies ○ Don't know	The desirable effects (decreased mortality + decreased length of stay) were judged to outweigh the undesirable effects (increased hyperglycemia), thereby favoring systemic corticosteroids in patients with severe CAP.
Acceptability Is the intervention acceptable to key stakeholders?	
JUDGEMENT	**RESEARCH EVIDENCE**
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	The intervention is most often delivered intravenously or via the gastrointestinal tract, which is acceptable to most patients. This is based on the committee's non-systematic clinical observations.
Feasibility Is the intervention feasible to implement?	
JUDGEMENT	**RESEARCH EVIDENCE**
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	The intervention is most often delivered intravenously or via the gastrointestinal tract, which is feasible in all hospitals. This is based on the committee's non-systematic clinical observations.

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SUMMARY OF JUDGEMENTS

	JUDGEMENT						
DESIRABLE EFFECTS	Trivial	Small	**Moderate**	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	**Favors the intervention**	Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
ACCEPTABILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention	Conditional recommendation against the intervention	Conditional recommendation for either the intervention or the comparison	**Conditional recommendation for the intervention**	Strong recommendation for the intervention
o	o	o	●	o

CONCLUSIONS

Recommendation

For hospitalized patients with severe community-acquired pneumonia, we suggest systemic corticosteroids (conditional recommendation, low quality of evidence).

Participation = 16/18 (89%)
Strong recommendation for systemic corticosteroids = 1/16 (6.25%).
Conditional recommendation for systemic corticosteroids =14/16 (87.50%).
Strong recommendations against systemic corticosteroids = 0/16 (0%).
Condition recommendation against systemic corticosteroids = 1/16 (6.25%).

B) Analysis #2: Patients Admitted to Ward

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QUESTION

Should hospitalized patients with severe community-acquired pneumonia received systemic corticosteroids rather than no systemic corticosteroids?	
POPULATION:	Hospitalized patients with **NON-SEVERE** community-acquired pneumonia
INTERVENTION:	Systemic corticosteroids
COMPARISON:	No systemic corticosteroids
SETTING:	Inpatients

ASSESSMENT

Desirable Effects

How substantial are the desirable effects? "Substantial" refers to both the importance of the outcomes and the magnitude of effect. As an example, a small improvement in a critical outcome might be more substantial than a large improvement in an unimportant outcome.

JUDGEMENT	**RESEARCH EVIDENCE**
● Trivial (if any) ○ Small ○ Moderate ○ Large ○ Varies ○ Don't know Beneficial effects are seen in heterogeneous populations of patients with CAP, but the effects appear to be driven by patients with severe CAP. There is no evidence of benefit in patients with non-severe CAP.	DESIRABLE EFFECTS <u>Decreased mortality:</u> CAP patients- 13 RCTs, 3575 patients, 6.1% versus 9.1% (NNT 33), RR 0.68, 95% CI 0.53-0.86. Severe CAP- 6 RCTs, 1634 patients, 9.8% versus 15.1% (NNT 19), RR 0.62, 95% CI 0.41-0.94. Non-severe CAP- 3 RCTs, 705 patients, 3.7% versus 5.1% (NNT 72) RR 0.73, 95% CI 0.36 to 1.46. <u>Decreased length of stay:</u> CAP patients- 12 RCTs, 3403 patients, MD -1.11 days, 95% CI -1.66 to -0.55 days. Severe CAP- 4 RCTs, 780 patients, MD -1.06 days, 95% CI -2.01 to -0.12 days. Non-severe CAP – 5 RCTs, 1556 patients, MD -0.61 days, 95% CI -1.36 to 0.14 days. RCT= randomized controlled trial, NNT= number needed to treat, RR = risk ratio, CI = confidence interval, MD = mean difference.

Undesirable Effects

How substantial are the undesirable effects? "Substantial" refers to both the importance of the outcomes and the magnitude of effect. As an example, a small increase in a critical adverse outcome might be more substantial than a large increase in an unimportant adverse outcome.

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JUDGEMENT	RESEARCH EVIDENCE
○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know The magnitude of the effect is small and it is average importance since it is treatable and reversible upon discontinuation.	UNDESIRABLE EFFECTS <u>Increased hyperglycemia:</u> CAP patients- 7 RCTs, 2476 patients, 14.5% versus 9% (NNH 18), RR 1.71, 95% 1.21-2.40. Severe CAP- no research evidence. Non-severe CAP- no research evidence. RCT= randomized controlled trial, NNH = number needed to harm, RR = risk ratio, CI = confidence interval.

Certainty of evidence
What is the committee's confidence in the accuracy of the above listed estimates (i.e., what is the quality of evidence)?

JUDGEMENT	RESEARCH EVIDENCE
○ Very low ● Low ○ Moderate ○ High ○ No included studies	QUALITY OF EVIDENCE The overall quality of evidence is determined by the lowest quality of evidence among critical outcomes. For the critical outcome of <u>mortality</u>, there is low-quality evidence because there are RCTs downgraded for risk of bias and imprecision.

Balance of effects
Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT	RESEARCH EVIDENCE
● Favors the comparison ○ Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors	The undesirable effects (increased hyperglycemia) outweigh the desirable effects (there might be no desirable effects in non-severe CAP), thereby favoring no systemic corticosteroids in patients with non-severe CAP.

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the intervention ○ Favors the intervention ○ Varies ○ Don't know	

Acceptability Is the intervention acceptable to key stakeholders?	
JUDGEMENT	**RESEARCH EVIDENCE**
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	The intervention is most often delivered intravenously or via the gastrointestinal tract, which is acceptable to most patients. This is based on the committee's non-systematic clinical observations.

Feasibility Is the intervention feasible to implement?	
JUDGEMENT	**RESEARCH EVIDENCE**
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	The intervention is most often delivered intravenously or via the gastrointestinal tract, which is feasible in all hospitals. This is based on the committee's non-systematic clinical observations.

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SUMMARY OF JUDGEMENTS

	JUDGEMENT						
DESIRABLE EFFECTS	**Trivial**	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Trivial	**Small**	Moderate	Large		Varies	Don't know
BALANCE OF EFFECTS	**Favors the comparison**	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	**Low**	Moderate	High			No included studies
ACCEPTABILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	**Yes**		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention ●	Conditional recommendation against the intervention ○	Conditional recommendation for either the intervention or the comparison ○	Conditional recommendation for the intervention ○	Strong recommendation for the intervention ○

CONCLUSIONS

Recommendation
For hospitalized patients with non-severe community-acquired pneumonia, we recommend NOT administering systemic corticosteroids (strong recommendation, low quality of evidence). Remark: The recommendation is strong despite the very low certainty of effects because the intent is to avoid harm due to unnecessary systemic corticosteroids.

Participation = 16/18 (89%)
Strong recommendations for systemic corticosteroids = 0/16 (0%).
Condition recommendation for systemic corticosteroids = 0/16 (0%).

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Strong recommendation against systemic corticosteroids = 13/16 (81.25%).
Conditional recommendation against systemic corticosteroids =3/16 (8.75%).

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