

Evidence Summary
Pediatric Community Acquired Pneumonia

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Objective: To critically review the evidence for pediatric community acquired pneumonia.

Inclusion Criteria:

- Patients between the ages of 60 days and 18 years
- Subpopulations of interest
 - Patients with asthma
 - Undervaccinated patients

Exclusion Criteria:

Patients with:

- Hospital-acquired pneumonia
- COVID-19
- Cystic Fibrosis and other chronic lung diseases
- Tracheostomy
- At risk for aspiration pneumonia
- Sickle Cell disease
- Pre-existing and/or congenital neurologic, hematologic, renal, metabolic, and cardiac conditions
- Immunodeficiency or immunosuppressive therapy

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Target Guideline Users: All clinicians caring for patients presenting within the OHSU Health System with proven or suspected CAP.

Quality Measures:

- Outcome
- Readmission rate
- Admission rate
- Cost of care per episode
- Patient experience

Outcomes for Evidence Review:

- Readmission
- Treatment-related adverse events
- LOS
- Surgical interventions
- Patient satisfaction and QOL
- ICU admission

Definitions:

- **Community-Acquired Pneumonia (CAP):** Pneumonia in a previously healthy child caused by an infection (predominantly *S. pneumoniae*, *S. aureus* [including methicillin-resistant *S. aureus*] and *S. pyogenes*)[1] that has been acquired outside of the hospital[2]
- **Hospital-Acquired Pneumonia (HAP):** Pneumonia not incubating at the time of hospital admission and occurring 48 hours or more after admission[3]
- **Complicated Pneumonia:** Pneumonia complicated by an empyema, progressing from an exudative effusion, to a fibrinopurulent stage with loculations, and then organized with a thick fibrinous peel
- **Uncomplicated Pneumonia:** Pneumonia in the absence of significant effusion, empyema, severe or impending respiratory failure, and/or signs and symptoms of sepsis or shock.

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Summary of Evidence

Question 1: When does a child or infant with CAP require hospitalization?

General consensus from literature and external guidelines

- Hospitalization
 - Moderate or severe CAP (**IDSA strong recommendation; moderate- to high-quality evidence**)
 - Respiratory distress
 - Age-adjusted tachypnea
 - <12 months: >55 to 70 breaths/min (*no consensus*)
 - 'Older children': >20 to 50 breaths/min (*no consensus*)
 - Dyspnea
 - Retractions (suprasternal, intercostals, or subcostal)
 - Grunting
 - Apnea
 - Nasal flaring
 - Hypoxemia (more frequent in severe CAP, variable in moderate) – pulse oximetric SpO₂ <90-93% in room air (*strong recommendation; some consensus on values*)
 - Infants less than 3 to 6 months of age (*strong recommendation; varying evidence on age and addition of suspected bacterial CAP*)
 - Suspected complicated CAP
 - Children who cannot be adequately cared for at home, unable to comply with therapy, unable to follow up
- Admission to ICU or continuous cardiorespiratory monitoring (**strong recommendation; moderate- to high-quality evidence**)
 - Invasive ventilation via nonpermanent artificial airway
 - Impending respiratory failure
 - Sustained tachycardia
 - Remains hypoxic on FiO₂ (*generally >50%; some consensus on value*)
 - Hypotension
 - Requires pharmacologic support of blood pressure or perfusion
 - Requires use of noninvasive positive pressure ventilation (CPAP or BiPAP)

Mentioned occasionally

- Comorbidities predisposing patient to more severe pneumonia (cardiopulmonary disease, malignancy, prematurity, chronic lung disease, immunocompromised)
- Inadequate oral intake or inability to tolerate PO (infant)
- Effusion
- Altered mental status (**IDSA strong recommendation; low-quality evidence**)
- Fever

- Failure of outpatient therapy
- Sepsis
- Severity of illness score indicating severe CAP (**strong recommendation; low-quality evidence**)
- Suspected or documented CAP caused by community-associated MRSA (**ISDA strong recommendation; low quality evidence**)
- Capillary refill time >2 min

Limitations for consideration

- No validated reference standard or scoring system for severity of CAP or need for hospitalization
- The ability of the family to comply with medical prescriptions is not always easy to establish
- No consensus on cutoff level of hypoxemia requiring hospitalization
- No consensus on age below which hospitalization should be required – and some caveat age limit, suggesting admit only for infants with suspected bacterial CAP

External Guidelines

In 2018, the **Canadian Paediatric Society** recommended the following:

- Most children with pneumonia can be managed as outpatients. Specific paediatric criteria for admission are not available.
- Hospitalization is generally indicated if a child has inadequate oral intake, is intolerant of oral therapy, has severe illness or respiratory compromise (eg, grunting, nasal flaring, apnea, hypoxemia), or if the pneumonia is complicated. There should be a lower threshold for admitting infants younger than six months of age to hospital because they may need more supportive care and monitoring, and it can be difficult to recognize subtle deterioration clinically.

In 2018, **New South Wales** recommended the following:

- The decision to hospitalize a child with pneumonia must be an individual one based on age and clinical factors.
- Hospitalization should be considered for all infants less than 3 months of age and for a child of any age whose family cannot provide appropriate care and assure compliance with the therapeutic plan.
- Additional indications for hospitalization include:
 - Hypoxaemia (oxygen saturation consistently less than 95% in room air)
 - Dehydration, or inability to maintain hydration orally; inability to feed in an infant
 - Moderate to severe respiratory distress:
 - Respiratory rate greater than 55 breaths/minute in infants less than 12 months, or respiratory rate greater than 50 breaths/minute in older children
 - Difficulty breathing, apnoea, or grunting
 - Signs of toxicity (drowsy, lethargic or irritable, pale, mottled and/or tachycardic)
 - Underlying conditions that may predispose to a more serious course of pneumonia such as cardiopulmonary disease, chronic lung disease, prematurity, history of malignancy

- Presence of complications (e.g. effusion/empyema)
- Failure of outpatient therapy (worsening or no response in 24 to 72 hours)

In 2017, the **American Academy of Pediatrics** recommended the following:

- Decisions on whether to hospitalize a patient are made by weighing the following criteria:
 - Hypoxemia (oxygen saturations <90% to 92% at sea level)
 - Infants <3 to 6 months of age with suspected bacterial community-acquired pneumonia
 - Tachypnea:
 - Infants <12 months of age: respiratory rate >70 breaths per min
 - Children: respiratory rate >50 breaths per min
 - Respiratory distress: apnea, grunting, difficulty breathing, and poor feeding
 - Signs of dehydration or inability to maintain hydration or oral intake
 - Capillary refill time >2 s
 - Infants and children with toxic appearance
 - Suspected or confirmed to have infection with a virulent organism (community-acquired methicillin-resistant *Staphylococcus aureus* or group A *Streptococcus*)
 - Underlying conditions/comorbidities that:
 - May predispose patients to a more serious course (eg, cardiopulmonary disease, genetic syndromes, neurocognitive disorders, neuromuscular disorders)
 - May be worsened by pneumonia (eg, metabolic disorder)
 - May adversely affect response to treatment (eg, immunocompromised host, sickle cell disease)
 - Complications (eg, effusion and/or empyema)
 - Failure of outpatient therapy (48–72 h with no clinical response)
 - Caretaker unable to provide appropriate observation or to comply with prescribed home therapy
- Indications for intensive care unit admission include:
 - Severe respiratory distress or impending respiratory failure that requires:
 - Intubation and mechanical ventilation
 - Positive pressure ventilation
 - Recurrent apnea or slow irregular respirations
 - Cardiopulmonary monitoring due to cardiovascular compromise secondary to:
 - Sustained tachycardia
 - Inadequate blood pressure
 - Requirement of pharmacological support for blood pressure or perfusion
 - Altered mental status due to hypercarbia or hypoxemia
 - Pulse oximetry measurement of <92% on fractional inspired oxygen concentration of >0.50
 - Pediatric Early Warning Score >6

In 2012, the **American Academy of Family Physicians** recommended:

- Infants



- Apnea or grunting
- Oxygen saturation $\leq 92\%$
- Poor feeding
- Respiratory rate > 70 breaths per minute
- Older children
 - Grunting
 - Inability to tolerate oral intake
 - Oxygen saturation $\leq 92\%$
 - Respiratory rate > 50 breaths per minute
- All age groups
 - Comorbidities (e.g., chronic lung disease, asthma, unrepaired or incompletely repaired congenital heart disease, diabetes mellitus, neuromuscular disease)
 - Family is not able to provide appropriate observation

In 2011, the **Pediatric Infectious Diseases Society and the Infectious Diseases Society of American (IDSA)** recommended the following:

- Children and infants who have moderate to severe CAP, as defined by several factors, including respiratory distress and hypoxemia (sustained saturation of peripheral oxygen, 90% at sea level) should be hospitalized for management, including skilled pediatric nursing care. **(strong recommendation; high-quality evidence)**
 - Signs of respiratory distress:
 - Tachypnea, respiratory rate, breaths/min
 - Age 0-2 months: >60
 - Age 2-12 months: >50
 - Age 1-5 years: >40
 - Age >5 years: >20
 - Dyspnea
 - Retractions (suprasternal, intercostals, or subcostal)
 - Grunting
 - Nasal flaring
 - Apnea
 - Altered mental status
 - Pulse oximetry measurement $<90\%$ on room air
- Infants less than 3–6 months of age with suspected bacterial CAP are likely to benefit from hospitalization. **(strong recommendation; low-quality evidence)**
- Children and infants with suspected or documented CAP caused by a pathogen with increased virulence, such as community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) should be hospitalized. **(strong recommendation; low-quality evidence)**
- Children and infants for whom there is concern about careful observation at home or who are unable to comply with therapy or unable to be followed up should be hospitalized. **(strong recommendation; low-quality evidence)**



- A child should be admitted to an ICU if the child requires invasive ventilation via a nonpermanent artificial airway (eg, endotracheal tube). **(strong recommendation; high-quality evidence)**
- A child should be admitted to an ICU or a unit with continuous cardiorespiratory monitoring capabilities if the child acutely requires use of noninvasive positive pressure ventilation (eg, continuous positive airway pressure or bilevel positive airway pressure). **(strong recommendation; very low-quality evidence)**
- A child should be admitted to an ICU or a unit with continuous cardiorespiratory monitoring capabilities if the child has impending respiratory failure. **(strong recommendation; moderate-quality evidence)**
- A child should be admitted to an ICU or a unit with continuous cardiorespiratory monitoring capabilities if the child has sustained tachycardia, inadequate blood pressure, or need for pharmacologic support of blood pressure or perfusion. **(strong recommendation; moderate-quality evidence)**
- A child should be admitted to an ICU if the pulse oximetry measurement is $<92\%$ on inspired oxygen of ≥ 0.50 . **(strong recommendation; low-quality evidence)**
- A child should be admitted to an ICU or a unit with continuous cardiorespiratory monitoring capabilities if the child has altered mental status, whether due to hypercarbia or hypoxemia as a result of pneumonia. **(strong recommendation; low-quality evidence)**
- Severity of illness scores should not be used as the sole criteria for ICU admission but should be used in the context of other clinical, laboratory, and radiologic findings. **(strong recommendation; low-quality evidence)**
 - Major criteria for CAP severity of illness:
 - Invasive mechanical ventilation
 - Fluid refractory shock
 - Acute need for NIPPV
 - Hypoxemia requiring FiO_2 greater than inspired concentration or flow feasible in general care area
 - Minor criteria for CAP severity of illness
 - Respiratory rate higher than WHO classification for age
 - Apnea
 - Increased work of breathing (e.g., retractions, dyspnea, nasal flaring, grunting)
 - PaO_2/FiO_2 ratio <250
 - Multilobar infiltrates
 - PEWS score >6
 - Altered mental status
 - Hypotension
 - Presence of effusion
 - Comorbid conditions (e.g., HgbSS, immunosuppression, immunodeficiency)
 - Unexplained metabolic acidosis



Primary Literature:

Source, Year	Summary of findings	Comments	Quality or risk of bias
Florin, 2018	<p>PIDS-IDSa criteria in predicting need for hospitalization (severe CAP) Sensitivity: 95% (89%) Specificity: 16% (46%) PPV: 67% (56%) NPV: 64% (85%) LR: 1.13 (1.65)</p> <p>Strongest predictors of NFH: non-invasive positive pressure ventilation, effusion, altered mental status, fluid refractory shock, multilobar infiltrates, low SpO₂:FiO₂ ratio, hypotension, metabolic acidosis, respiratory rate >WHO criteria, pediatric early warning score >6</p> <p>Strongest predictors of severe CAP: hypoxemia, altered mental status, pediatric early warning score >6, increased work of breathing, hypotension, respiratory rate >WHO criteria</p>	<ul style="list-style-type: none"> • PIDS-IDSa criteria fair to good ability to discriminate severity of CAP, but not need for hospitalization • Many criteria lack reliability and interpretation of criteria is variable 	<p>Low to unclear risk of bias^a</p> <ul style="list-style-type: none"> • Note: Retrospective cohort (N=518) in one peds ED

^a QUADAS-2 tool for diagnostic accuracy studies

*No systematic reviews, RCTs, or prospective cohorts available, therefore retrospective cohort presented.

Abbreviations: LR = likelihood ratio; NPV = negative predictive value; PPV = positive predictive value

Quality of evidence (GRADE)

Risk of bias	Imprecision	Inconsistency	Indirectness	Publication bias	Certainty (Overall)
Low	Imprecise	Inconsistent	Direct	No	Low to Moderate

Certainty: Low to moderate suggests future research will likely have an important impact on confidence in the estimate of effect and may change the estimate. See Appendix A for more information.

Question 2: What diagnostic laboratory and imaging tests should be used in a child with suspected CAP in a clinic or hospital ward setting?

General consensus from literature and external guidelines

- A moving target, largely reliant on clinical judgment, plus imaging and laboratory tests for those admitted to hospital
- No true gold standard as a diagnostic reference
 - CXR exposes children to radiation, normal reading does not exclude pneumonia, limited relevance to clinical outcomes; ultrasound easier and less costly, but interpretation is dependent on expertise of reader, cannot image entire lung at once, and consolidation can be missed (if deep) or misinterpreted (spleen, air in the stomach)
 - Lab tests may be contaminated by other organisms not responsible for pneumonia, cultures may have low yield and therefore high cost per case, sensitivity / specificity may be limited
- Patients managed in outpatient setting
 - Most laboratory and imaging tests are not routinely indicated in outpatient management (**strong recommendation; high-quality evidence**)
 - Blood cultures may be considered upon failure of outpatient therapy (*some consensus*)
- Patients admitted for hospitalization
 - Pulse oximetry
 - Should be performed in all children with CAP and suspected hypoxemia (**strong recommendation; high-quality evidence**)
 - Imaging
 - Ultrasonography is preferred first line imaging (**strong recommendation; moderate-quality evidence**)
 - Easier, can be done in sleeping children, but interpretation dependent on expertise of reader
 - Chest radiographs (CXR; postero-anterior and lateral) may be obtained in hospitalized patients to document presence, size, and character of infiltrates and verify absence or presence of complications (*some consensus*)
 - Follow-up CXR not routinely indicated, unless progressive symptoms or clinical deterioration 48-72 hours after initiation of therapy (**strong recommendation; moderate-quality evidence**)
 - Blood cultures
 - Not routinely indicated
 - Consider with children admitted with CAP that have pleural effusion or require ICU admission
 - Repeat cultures not routinely indicated, unless bacteremia caused by *S. aureus*
 - Microbiological and virological tests
 - Should test for influenza virus in all children with CAP (**strong recommendation**)
 - In children with signs and symptoms suspicious for *M. pneumoniae*, consider testing to help guide antibiotic selection
 - Acute phase reactants

- In children with moderate to severe CAP, serum procalcitonin, ESR, and CRP may be used to inform clinical management along with other laboratory and imaging studies
- CBC
 - Not routinely indicated, but may consider for children with severe CAP along with other laboratory and imaging studies
- Sputum Gram stain and cultures
 - May be obtained for children who can provide sufficient sputum
- Urinary antigen detection tests
 - Not indicated (**strong recommendation**)
- Patients who are critically ill
 - Chest CT with contrast for necrotizing pneumonia and lung abscesses
 - Tracheal aspirates for Gram stain and culture and viral pathogens in intubated children
 - Bronchoscopy, bronchoalveolar lavage, or biopsy only if other diagnostic tests are negative

Limitations for consideration

- A universally accepted, practical reference standard for diagnosis of pneumonia does not exist
- The future of CXR is uncertain; ultrasound is preferred, but utility for informing antibiotic treatment is less well-studied
- Pathogen detection is limited by potential contamination of other colonizing pathogens or multiple infection sources, limited sensitivity and/or specificity, and difficulty in differentiating bacterial vs. viral pneumonia

External Guidelines

In 2018, the **Canadian Paediatric Society** recommended the following:

- Optimally, the diagnosis of bacterial pneumonia should be supported by a chest radiograph before starting antimicrobials. When bacterial pneumonia is suspected clinically (a febrile child with acute respiratory symptoms and physical findings compatible with consolidation or pleural effusion), a chest radiograph (both postero-anterior and lateral) should usually be obtained.
 - Radiographs are not indicated for children experiencing wheezing with a typical presentation of bronchiolitis or asthma because bacterial pneumonia is very unlikely. However, in cases where the diagnosis of bacterial pneumonia is highly suspected from history, combined with typical clinical and physical findings and the child is not sufficiently ill to require hospitalization, a chest radiograph is not essential.
 - Ultrasound at the point of care appears to be sensitive and specific for detecting pneumonic infiltrates but requires further validation.
- Most cases are not bacteremic at the time of diagnosis. If sputum is available (usually only in children >10 years of age), it should be sent for Gram staining and, if considered adequate, cultured.



- Viral testing of nasopharyngeal secretions is usually not indicated for outpatients with suspected pneumonia. However, such testing should be strongly considered in children admitted during influenza season with possible viral pneumonia because antivirals are likely to be of benefit for influenza pneumonia, particularly in moderately to severely ill children.
 - Nasopharyngeal specimens should be sent for molecular diagnostics if testing is available and the child is hospitalized, bearing in mind that the length of carriage is unknown; a positive result may indicate remote infection.
- A complete blood count with differential testing and blood cultures (before starting antimicrobial therapy, if possible) are indicated for children who are hospitalized. Even though the yield from blood cultures is low, a positive result is helpful, especially if the child subsequently experiences a complicated course.
 - As adequate volumes of blood are more likely to yield a pathogen, the minimum volume of blood cultured should be at least 1 mL to 2 mL in infants, 4 mL to 5 mL in children <10 years of age and 10 mL to 20 mL in older children.

In 2018, **New South Wales** recommended the following:

- The diagnosis of pneumonia requires historical or physical examination evidence of an acute infectious process with signs or symptoms of respiratory distress or radiologic evidence of an acute pulmonary infiltrate, and depends to some extent upon the setting (inpatient or outpatient), the severity of the illness, and the age of the patient.
 - In general, aetiologic diagnosis should be sought in children who require admission to hospital and those who fail to respond to initial treatment.
- In appropriate clinical setting the diagnosis can be made without radiographs. Chest x-ray changes may lag behind clinical findings and ultrasound.
 - Children that are well enough to be discharged from the ED with clear clinical signs of pneumonia do not need a chest x-ray to confirm the diagnosis. In children with mild CAP, a chest x-ray should not be considered a routine test.
- It is recommended that a chest x-ray be obtained when:
 - Pneumonia is classified as moderate to severe
 - Clinical findings are unclear
 - Exclusion of alternate explanation for respiratory distress (foreign body, heart failure)
 - A complication such as pleural effusion is suspected
 - The pneumonia is prolonged or unresponsive to antimicrobials
 - In a rural setting where access to after-hours diagnostics is limited, or decisions regarding escalation of care need to be made early.
- In children with severe CAP, the diagnosis should be confirmed by chest x-ray and a full investigative process undertaken. Most children that require hospital admission will have moderate to severe disease and will require a chest x-ray.
 - The recommended chest x-ray view depends upon the age of the child.
 - In children older than 4 years the front posterior upright chest view is usually obtained to minimize the cardiac shadow.
 - In younger children the position does not affect the cardiothoracic shadow, and the anterior-posterior supine view is preferred.

- Lateral chest x-ray should not be routinely performed.
- Ultrasound is simple, radiation-free, more sensitive than chest x-ray for detection of CAP in children, and is as good as chest x-ray in identifying pleuropulmonary alterations in children with suspected pneumonia.
 - Indicated as first line investigation to confirm and quantify pleural fluid and empyema if suspected clinically or radiologically
- Continuous pulse oximetry should be performed in every child that presents with CAP.
- Laboratory evaluation of the child with CAP depends on the clinical scenario, age, severity of illness, presence of potential complications, underlying comorbidities, and requirement for admission.
 - As a general rule children who are managed as outpatients do not require any investigations unless significant comorbidities.
 - Young infants (i.e. less than 3 months) in whom pneumonia is suspected, particularly those who are febrile and have signs of toxicity, will require further investigation to exclude other causes of infection.
 - Complete blood count:
 - In children with mild CAP, not necessary unless significant comorbidities.
 - In children with moderate CAP, it may be considered as it may provide useful information in conjunction with the clinical presentation to allow a decision to be made regarding requirement for admission to hospital.
 - In children admitted with severe CAP, should be undertaken.
 - Acute phase reactants: ESR, CRP, and serum procalcitonin should only be considered in moderate to severe disease, and may be used in conjunction with clinical findings to assess response to therapy.
 - Full blood count: Look for neutrophilia, leucopaenia, and lymphocytosis
 - Urea and electrolytes: In moderate to severe disease only, urinal and electrolyte testing may be helpful in assessing the degree of dehydration and whether hyponatraemia is present
 - Microbiological investigations: For children admitted to hospital with CAP it is important to attempt a microbiological diagnosis
 - Blood culture: Should be obtained if the child requires admission to hospital, in children with moderate to severe CAP
 - Repeat cultures of *S. aureus* should be performed every 24 hours until they are 'no growth' to document efficacy of therapy; this should occur regardless of clinical status and antimicrobial therapy should continue for the full duration
 - Sputum Gram stain and culture: reasonable sensitivity and specificity for presumptive detection of *S. pneumoniae*
 - Nasopharyngeal bacterial culture: uninformative and should not be routinely undertaken
 - Nasopharyngeal aspirates: Should be considered for viral detection using PCR and/or immunofluorescence on all children less than 18 months admitted with CAP.
 - Pleural fluid: if required expertise is available, may be used for diagnostic purposes when there is evidence of effusion present
 - Urine: should not be undertaken, as specificity is too poor

- Serum: If patient is admitted with severe pneumonia or clinical presentation is supportive of an infection with Mycoplasma or Chlamydia
 - Serology remains the mainstay for diagnosing M. pneumoniae and C. pneumoniae

In 2017, the **American Academy of Pediatrics** recommended the following:

- Focal opacity on chest radiographs is often held as a standard of reference; however, some viral processes and atelectasis can cause focal radiographic findings (though atelectasis traditionally resolves in 48–72 hours), and findings on radiographs can lag behind clinical symptoms. No standard of reference for diagnosis or single definition of pneumonia exists.
 - Unfortunately, no constellation of clinical symptoms or signs (fever, tachypnea, hypoxemia, work of breathing) displays good specificity or sensitivity for radiographic findings of pneumonia, except that symptom severity and ill appearance do correlate with focal infiltrates.
- Chest radiographs are indicated in patients with more severe respiratory distress, particularly those who meet criteria for hospitalization.
 - Other indications for chest radiography include inconclusive clinical findings and ruling out other possible causes of respiratory distress that can be diagnosed at radiography (foreign body, pneumothorax, pleural disease, or cardiac disease, including pulmonary edema and cardiomegaly).
 - Imaging is also indicated in febrile infants without a source who are younger than 12 months of age, if there is evidence of leukocytosis.
- Conversely, in patients with mild evidence of lower respiratory tract infection (fever, cough) without hypoxemia or a focal lung examination who are stable for outpatient treatment, radiographs of the chest are not typically indicated. In addition, it is not recommended to pursue tests to assess for a cause if the patient does not meet criteria for inpatient treatment.
- Laboratory examinations are considered for all patients ill enough to be hospitalized with suspected bacterial pneumonia. The number and types of examinations performed depends on the severity and trajectory of the illness. These may commonly include blood cultures, inflammatory markers, complete blood cell count, and nasopharyngeal swab PCR for viruses.
 - Blood cultures rarely yield positive findings in CAP, and they should not be performed in patients treated on an outpatient basis or in hospitalized patients with uncomplicated disease.
 - When pleural fluid is obtained, it should be sent for Gram stain and bacterial culture, as well as cell count and differential, to allow differentiation of bacteria from other causes of effusion (ie, mycobacterial, oncologic).
 - Inflammatory markers (erythrocyte sedimentation rate, C-reactive protein level, or procalcitonin) may aid in clinical decision-making if measured longitudinally, particularly in those with complicated CAP.
 - The complete blood cell count may provide information on further complications, such as thrombocytopenia or anemia from hemolytic uremic syndrome.
 - Nasopharyngeal swabs for viral PCR should only be performed if the results will change management.

- Coordination with a respiratory therapist to use specialized techniques to improve sputum expectoration and/or nasal aspiration may be required in children younger than 6 years of age to obtain a successful, high-quality specimen (fewer than 10 squamous epithelial cells per low-power field). While sputum collection is not necessary for evaluation in a patient treated on an outpatient basis, attempts should be made to obtain sputum in children with moderate to severe pneumonia who are hospitalized.

In 2017 the **American Academy of Pediatrics Section on Emergency Medicine Committee on Quality Transformation** recommended the following:

- In the ED setting, for children with mild CAP:
 - CBC, inflammatory markers, blood cultures not routinely indicated
 - Imaging not routinely indicated; consider CXR in those with diagnostic uncertainty or concern for complications
- In the ED setting, for children with moderate CAP:
 - CBC, inflammatory markers not routinely indicated
 - Blood culture not routinely indicated unless complicated pneumonia or underimmunized child
 - Obtain AP and lateral chest x-ray; consider bedside ultrasound as adjunct diagnostic tool if ultrasound credentialed provider is present
- In the ED setting, for children with severe CAP:
 - Obtain CBC/differential
 - Consider inflammatory markers (ESR, CRP), lactate, VBG, and BMP
 - Obtain blood and sputum culture (if able to expectorate)
 - Obtain AP and lateral chest x-ray; consider bedside ultrasound as adjunct diagnostic tool if ultrasound credentialed provider is present

In 2016, the **American College of Emergency Physicians** recommended the following:

- In well-appearing immunocompetent infants and children aged 2 months to 2 years presenting with fever ($\geq 38^{\circ}\text{C}$ [100.4°F]) and no obvious source of infection, physicians should consider obtaining a chest radiograph for those with cough, hypoxia, rales, high fever ($\geq 39^{\circ}\text{C}$), fever duration greater than 48 hours, or tachycardia and tachypnea out of proportion to fever. (**Level B recommendation**)
- In well-appearing immunocompetent infants and children aged 2 months to 2 years presenting with fever ($\geq 38^{\circ}\text{C}$ [100.4°F]) and wheezing or a high likelihood of bronchiolitis, physicians should not order a chest radiograph. (**Level C recommendation**)

In 2011, the **Pediatric Infectious Diseases Society and the Infectious Diseases Society of American (IDSA)** recommended the following:

Microbiologic Testing

Blood Cultures: Outpatient

- Blood cultures should not be routinely performed in nontoxic, fully immunized children with CAP managed in the outpatient setting. (**strong recommendation; moderate-quality evidence**)

- Blood cultures should be obtained in children who fail to demonstrate clinical improvement and in those who have progressive symptoms or clinical deterioration after initiation of antibiotic therapy. **(strong recommendation; moderate-quality evidence)**

Blood Cultures: Inpatient

- Blood cultures should be obtained in children requiring hospitalization for presumed bacterial CAP that is moderate to severe, particularly those with complicated pneumonia. **(strong recommendation; low-quality evidence)**
- In improving patients who otherwise meet criteria for discharge, a positive blood culture with identification or susceptibility results pending should not routinely preclude discharge of that patient with appropriate oral or intravenous antimicrobial therapy. The patient can be discharged if close follow-up is assured. **(weak recommendation; low-quality evidence)**

Follow-up Blood Cultures

- Repeated blood cultures in children with clear clinical improvement are not necessary to document resolution of pneumococcal bacteremia. **(weak recommendation; low-quality evidence)**
- Repeated blood cultures to document resolution of bacteremia should be obtained in children with bacteremia caused by *S. aureus*, regardless of clinical status. **(strong recommendation; low-quality evidence)**

Sputum Gram Stain and Culture

- Sputum samples for culture and Gram stain should be obtained in hospitalized children who can produce sputum. **(weak recommendation; low-quality evidence)**

Urinary Antigen Detection Tests

- Urinary antigen detection tests are not recommended for the diagnosis of pneumococcal pneumonia in children; false-positive tests are common. **(strong recommendation; high-quality evidence)**

Testing For Viral Pathogens

- Sensitive and specific tests for the rapid diagnosis of influenza virus and other respiratory viruses should be used in the evaluation of children with CAP. A positive influenza test may decrease both the need for additional diagnostic studies and antibiotic use, while guiding appropriate use of antiviral agents in both outpatient and inpatient settings. **(strong recommendation; high-quality evidence)**
- Antibacterial therapy is not necessary for children, either outpatients or inpatients, with a positive test for influenza virus in the absence of clinical, laboratory, or radiographic findings that suggest bacterial coinfection. **(strong recommendation; high-quality evidence)**
- Testing for respiratory viruses other than influenza virus can modify clinical decision making in children with suspected pneumonia, because antibacterial therapy will not routinely be required for these children in the absence of clinical, laboratory, or radiographic findings that suggest bacterial coinfection. **(weak recommendation; low-quality evidence)**

Testing for Atypical Bacteria

- Children with signs and symptoms suspicious for *Mycoplasma pneumoniae* should be tested to help guide antibiotic selection. **(weak recommendation; moderate-quality evidence)**
- Diagnostic testing for *Chlamydia pneumoniae* is not recommended as reliable and readily available diagnostic tests do not currently exist. **(strong recommendation; high-quality evidence)**

Ancillary Diagnostic Testing

Complete Blood Cell Count

- Routine measurement of the complete blood cell count is not necessary in all children with suspected CAP managed in the outpatient setting, but in those with more serious disease it may provide useful information for clinical management in the context of the clinical examination and other laboratory and imaging studies. **(weak recommendation; low-quality evidence)**
- A complete blood cell count should be obtained for patients with severe pneumonia, to be interpreted in the context of the clinical examination and other laboratory and imaging studies. **(weak recommendation; low-quality evidence)**

Acute-Phase Reactants

- Acute-phase reactants, such as the erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) concentration, or serum procalcitonin concentration, cannot be used as the sole determinant to distinguish between viral and bacterial causes of CAP. **(strong recommendation; high-quality evidence)**
- Acute-phase reactants need not be routinely measured in fully immunized children with CAP who are managed as outpatients, although for more serious disease, acute-phase reactants may provide useful information for clinical management. **(strong recommendation; low-quality evidence)**
- In patients with more serious disease, such as those requiring hospitalization or those with pneumonia-associated complications, acute-phase reactants may be used in conjunction with clinical findings to assess response to therapy. **(weak recommendation; low-quality evidence)**

Pulse Oximetry

- Pulse oximetry should be performed in all children with pneumonia and suspected hypoxemia. The presence of hypoxemia should guide decisions regarding site of care and further diagnostic testing. **(strong recommendation; moderate-quality evidence)**

Chest Radiography

Initial Chest Radiographs: Outpatient

- Routine chest radiographs are not necessary for the confirmation of suspected CAP in patients well enough to be treated in the outpatient setting (after evaluation in the office, clinic, or emergency department setting). **(strong recommendation; high-quality evidence)**

- Chest radiographs, posteroanterior and lateral, should be obtained in patients with suspected or documented hypoxemia or significant respiratory distress and in those with failed initial antibiotic therapy to verify the presence or absence of complications of pneumonia, including parapneumonic effusions, necrotizing pneumonia, and pneumothorax. **(strong recommendation; moderate-quality evidence)**
 - Signs of respiratory distress:
 - Tachypnea, respiratory rate, breaths/min
 - Age 0-2 months: >60
 - Age 2-12 months: >50
 - Age 1-5 years: >40
 - Age >5 years: >20
 - Dyspnea
 - Retractions (suprasternal, intercostals, or subcostal)
 - Grunting
 - Nasal flaring
 - Apnea
 - Altered mental status
 - Pulse oximetry measurement <90% on room air

Initial Chest Radiographs: Inpatient

- Chest radiographs (posteroanterior and lateral) should be obtained in all patients hospitalized for management of CAP to document the presence, size, and character of parenchymal infiltrates and identify complications of pneumonia that may lead to interventions beyond antimicrobial agents and supportive medical therapy. **(strong recommendation; moderate-quality evidence)**

Follow-up Chest Radiograph

- Repeated chest radiographs are not routinely required in children who recover uneventfully from an episode of CAP. **(strong recommendation; moderate-quality evidence)**
- Repeated chest radiographs should be obtained in children who fail to demonstrate clinical improvement and in those who have progressive symptoms or clinical deterioration within 48–72 hours after initiation of antibiotic therapy. **(strong recommendation; moderate-quality evidence)**
- Routine daily chest radiography is not recommended in children with pneumonia complicated by parapneumonic effusion after chest tube placement or after videoassisted thoracoscopic surgery (VATS), if they remain clinically stable. **(strong recommendation; low-quality evidence)**
- Follow-up chest radiographs should be obtained in patients with complicated pneumonia with worsening respiratory distress or clinical instability, or in those with persistent fever that is not responding to therapy over 48-72 hours. **(strong recommendation; low-quality evidence)**
- Repeated chest radiographs 4–6 weeks after the diagnosis of CAP should be obtained in patients with recurrent pneumonia involving the same lobe and in patients with lobar collapse at initial chest radiography with suspicion of an anatomic anomaly, chest mass, or foreign body aspiration. **(strong recommendation; moderate-quality evidence)**



What Additional Diagnostic Tests Should Be Used in a Child with Severe or Life-Threatening CAP?

- The clinician should obtain tracheal aspirates for Gram stain and culture, as well as clinically and epidemiologically guided testing for viral pathogens, including influenza virus, at the time of initial endotracheal tube placement in children requiring mechanical ventilation. **(strong recommendation; lowquality evidence)**
- Bronchoscopic or blind protected specimen brush sampling, bronchoalveolar lavage (BAL), percutaneous lung aspiration, or open lung biopsy should be reserved for the immunocompetent child with severe CAP if initial diagnostic tests are not positive. **(weak recommendation; low-quality evidence)**

Primary literature evidence (highest level of evidence*)

Source, Year	Study (N)	Summary of findings	Quality ^a
Orso, 2018	Systematic review (2,612; k=17)	<ul style="list-style-type: none"> • Pooled sensitivity: 94% (89% to 97%) • Pooled specificity: 94% (86% to 98%) • AUC: 0.98 (IQR 0.94 to 0.99) <p>CXR as reference</p> <ul style="list-style-type: none"> • Sensitivity: 91% (81% to 96%) • Specificity: 84% (64% to 94%) <p>Clinical dx as reference</p> <ul style="list-style-type: none"> • Sensitivity: 98% (94% to 100%) • Specificity: 99% (96% to 100%) <p>Adjudication as reference</p> <ul style="list-style-type: none"> • Sensitivity: 96% (85% to 99%) • Specificity: 98% (86% to 100%) • Note: high heterogeneity in studies; results may not be reliable; findings similar to other SRs (e.g., Xin 2018) 	Good ^b
Omran, 2018	Prospective cohort (50)	In patients <1 year old	Low to unclear risk of bias

		<ul style="list-style-type: none"> • Sensitivity / Specificity: 98% / 91% • PPV: 98% • NPV: 91% 	
Stockmann, 2018	Prospective cohort (N=532)	<p>Odds of ICU admission</p> <ul style="list-style-type: none"> • Procalcitonin <0.25 ng/mL: aOR 0.48 (0.30 to 0.78) <p>Typical bacterial infections <i>PCT <2 ng/mL</i></p> <ul style="list-style-type: none"> • Sensitivity / Specificity: 61% / 79% • PPV: 0.28 • NPV: 0.94 • LR 2.92 <p>Atypical bacterial infections <i>PCT <0.25 ng/mL</i></p> <ul style="list-style-type: none"> • Sensitivity / Specificity: 85% / 45% • NPV: 0.96 • AUC: 0.80 	Low to unclear risk of bias
Alcoba, 2017	Prospective cohort (N=142)	<p>Pneumonia</p> <ul style="list-style-type: none"> • Procalcitonin >2 ng/mL: OR 4.2 (1.2 to 5.9) • CRP >80 mg/L: 6.4 (2.9 to 13.9) • Clinical mode: OR 2.6 (1.2 to 5.9) • Procalcitonin + clinical mode: OR 3.8 (1.8 to 8) • CRP + clinical mode: OR 5.04 (2.4 to 10.8) <p>Complicated pneumonia</p> <ul style="list-style-type: none"> • Procalcitonin >2 ng/mL: OR 	Low risk of bias



		<p>5.5 (2.1 to 14.4)</p> <ul style="list-style-type: none"> • CRP >80 mg/L: OR 22.7 (5.1 to 101.4) • Clinical mode: OR 5 (1.7 to 14.6) • Procalcitonin + clinical mode: OR 7.1 (2.8 to 17.7) • CRP + clinical mode: OR 23.5 (7.4 to 75.1) <p><i>Procalcitonin >2 ng/mL</i></p> <ul style="list-style-type: none"> • Sensitivity / Specificity: 67.4% / 67.1% • PPV / NPV: 55.9% / 76.8% LR: 2.04 <p><i>CRP >80 mg/L</i></p> <ul style="list-style-type: none"> • Sensitivity / Specificity: 73.5% / 69.7% • PPV / NPV: 58.1% / 82.2% LR: 2.43 <p><i>Clinical mode (wheezing absent, hypoventilation, grunting)</i></p> <ul style="list-style-type: none"> • Sensitivity / Specificity: 72% / 49% • LR: 1.4 <p>Complicated pneumonia</p> <p><i>Procalcitonin >2 ng/mL</i></p> <ul style="list-style-type: none"> • Sensitivity: 67.4% • Specificity: 67.1% • PPV: 55.9% • NPV: 76.8% LR: 2.04 <p><i>CRP >80 mg/L</i></p>	
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		<ul style="list-style-type: none"> • Sensitivity: 73.5% • Specificity: 69.7% • PPV: 58.1% • NPV: 82.2% • LR: 2.43 <p><i>Clinical mode (wheezing absent, hypoventilation, grunting)</i></p> <ul style="list-style-type: none"> • Sensitivity / Specificity: 84.6% / 47.4% • LR: 1.6 <p>*CXR as reference standard</p>	
Nascimento-Carvalho, 2010	Prospective cohort (159)	<p>Bacteremic vs. viral pneumonia <i>Procalcitonin ≥ 2 ng/mL</i></p> <ul style="list-style-type: none"> • OR 6.72 (1.20 to 37.59) • Sensitivity / Specificity: 75% / 66% • PPV: 24% • NPV: 95% • AUC: 0.80 	Low risk of bias
Fritz, 2019	Prospective cohort (2,143)	<ul style="list-style-type: none"> • Causative pathogen identified with BC: 2.2% • Hospital LOS: aHR 0.79 (0.73 to 0.86) • ICU admission: aOR 5.12 (3.82 to 6.84) • IMV and/or shock: aOR 5.28 (2.41 to 11.57) • NNC admitted patients with no effusion: 91 • NNC for ICU admission: 24 	Low risk of bias



		<ul style="list-style-type: none"> • NNC admitted patients with parapneumonic effusion: 12 <p>Factors associated with non-bacteremic pneumonia vs. bacteremic pneumonia</p> <ul style="list-style-type: none"> • Chest indrawing (54% vs. 35%) • Wheezing (40% vs. 24%) • PaO₂:FiO₂ ratio (451 vs. 462) • Procalcitonin ng/mL (0.32 vs. 4.1) • Parapneumonic effusion on CXR (12% vs. 48%) • Empyema with drainage procedure (4% vs. 17%) • Hospital LOS (2.8 days vs. 5.8 days) • ICU admission (21% vs. 43%) 	
Iroh Tam, 2015	Systematic review (N=8,621, k=21)	<ul style="list-style-type: none"> • Overall pooled prevalence: 5.14% (3.61 to 7.28), I²=91.3% • Adjusted for publication bias: 4.71% (3.07 to 6.34) • Severe CAP pooled prevalence: 9.89% (6.79 to 14.19) • Non-severe CAP pooled prevalence: 	Moderate ^b



		<p>4.17% (2.79 to 6.18)</p> <ul style="list-style-type: none"> • Children with CAP had positive blood cultures in 5.14% of cases (adjusted prevalence 4.7%) • Positive BC rates varied by type of study, geography, pre- vs. post-PCV, and CAP severity • Studies focusing on severe CAP had highest effect estimates and lowest heterogeneity in results, supporting the case for BC in severe CAP only 	
Stockmann, 2018	Diagnostic Study (N=532)	<ul style="list-style-type: none"> • Patients with typical bacteria had higher PCT concentrations (\pmviruses; n = 54; median, 6.10; IQR, 0.84-22.79 ng/mL) than those with atypical bacteria (\pmviruses; n = 82; median, 0.10; IQR, 0.06-0.39 ng/mL), viral pathogens only (n = 349; median, 0.33; 	Moderate



		<p>IQR, 0.12-1.35 ng/mL), or no pathogen detected (n = 47; median, 0.44; IQR, 0.10-1.83 ng/mL) (P < .001 for all).</p> <ul style="list-style-type: none"> No child with PCT <0.1 ng/mL had typical bacteria detected. Procalcitonin <0.25 ng/mL featured a 96% negative predictive value (95% confidence interval [CI], 93-99), 85% sensitivity (95% CI, 76-95), and 45% specificity (95% CI, 40-50) in identifying children without typical bacterial CAP. CONCLUSIONS: Lower PCT concentrations in children hospitalized with CAP were associated with a reduced risk of typical bacterial detection and may help identify children who would not benefit from 	
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		antibiotic treatment.	
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^a QUADAS-2 tool for diagnostic accuracy studies

^b AMSTAR tool for systematic reviews

*Systematic reviews, RCTs, prospective cohorts only. Lower levels of evidence presented in detailed evidence section.

Abbreviations: I^2 = index of heterogeneity, with values above 40-50% indicating higher heterogeneity among studies and thus less reliable estimates; LR = likelihood ratio; NPV = negative predictive value; PPV = positive predictive value

Lower levels of evidence:

Source, Year	Study (N)	Summary of findings	Quality
Alcoba, 2015	Secondary analysis of prospective cohort (N=88)	<p>Discriminating complicated vs. non-complicated CAP</p> <ul style="list-style-type: none"> • ProADM: OR 6.67 (1.7 to 25.3) • CRP: 75.6 (4.2 to 1348) <p>Discriminating bacteremic vs. non-bacteremic CAP</p> <ul style="list-style-type: none"> • ProADM: OR 20.8 (1.1 to 400.5) <p>CRP: OR 21.3 (1.1 to 411)</p> <p>Complicated vs. non-complicated CAP <i>ProADM >0.16 nmol/L</i> Sensitivity / Specificity: 72.7% / 71.4% LR: 2.55 ROC: 0.72 <i>CRP > 100 mg/L</i> Sensitivity / Specificity: 100% / 77% LR: 4.1 ROC: 0.89</p> <p>Bacteremic vs. non-bacteremic CAP <i>ProADM >0.16 nmol/L</i> Sensitivity / Specificity: 100% / 70% LR: 2.98 ROC: 0.85 <i>CRP > 100 mg/L</i></p>	Unclear to high risk of bias



		Sensitivity / Specificity: 100% / 70% LR: 3.03 ROC: 0.85	
Hoshina, 2014	Retrospective cohort (N=54)	Bacterial vs. non-bacterial pneumonia <i>Procalcitonin >0.2 ng/mL</i> AUC: 0.87 Sensitivity / Specificity: 86% / 80% <i>CRP >5.73 mg/dL</i> AUC: 0.76 Sensitivity / Specificity: 71% / 80%	Low to high risk of bias
Andrews, 2015	Cost-effectiveness analysis	<ul style="list-style-type: none"> • NNC to identify 1 patient with bacteremia, resulting in meaningful antibiotic change, if screen all admitted patients: 122 • NNC only in high risk patients: 42 <p>Patients at high risk for bacteremia</p> <ul style="list-style-type: none"> • <6 months with fever or not fully immunized • Have a central line • Are immunocompromised • Appear toxic or admitted to ICU • Chronic medical condition • Effusion or empyema on CXR 	NA



Principi, 2017	Literature review	<ul style="list-style-type: none"> • Areas can be obscured by anatomy if CXR only postero-anterior or antero-posterior, but two projections increases radiation exposure • LUS fast, can be performed at the bedside, radiation-free, and can be used to monitor evolution of consolidation and effusion • However, LUS methods are not standardized, diagnosis of interstitial CAP is less accurate than CXR (although as this is viral, importance of this limitation is lower), better at detecting small consolidations but the clinical importance of this is uncertain, and importance for clinical outcomes is still under investigation. 	NA
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Quality of evidence (GRADE) – Ultrasonography

Risk of bias	Imprecision	Inconsistency	Indirectness	Publication bias	Certainty (Overall)
Moderate	Precise	Consistent	Direct	No	Moderate

Note: Moderate suggests future research will likely have an important impact on confidence in the estimate of effect and may change the estimate.

Quality of evidence (GRADE) – Blood Cultures

Risk of bias	Imprecision	Inconsistency	Indirectness	Publication bias	Certainty (Overall)
Moderate	Precise	Consistent	Direct	No	Moderate

Note: Moderate suggests future research will likely have an important impact on confidence in the estimate of effect and may change the estimate.

Quality of evidence (GRADE) – Biomarkers

Risk of bias	Imprecision	Inconsistency	Indirectness	Publication bias	Certainty (Overall)
Moderate	Imprecise	Inconsistent	Direct	No	Low

Note: Low suggests future research will have an important impact on confidence in the estimate of effect and will likely change the estimate.

Quality of evidence (GRADE) – Procalcitonin

Risk of bias	Imprecision	Inconsistency	Indirectness	Publication bias	Certainty (Overall)
Moderate	Imprecise	Inconsistent	Direct	No	Low

Note: Low suggests future research will have an important impact on confidence in the estimate of effect and will likely change the estimate.

Question 3: Which anti-infective therapy should be provided to a child with suspected CAP in both the outpatient and inpatient settings?

General consensus from literature and external guidelines

- Outpatient
 - Mild
 - Amoxicillin as a first-line therapy for preschool children and school-aged children and adolescents with mild to moderate CAP for infants suspected to be of bacterial origin (**Strong Recommendation; Moderate Quality Evidence**)
 - Macrolide antibiotics should be prescribed for treatment of children (primarily school-aged children and adolescents) with mild to moderate CAP caused by atypical pathogens (**Conditional Recommendation; Moderate Quality Evidence – IDSA Guideline**)
 - If suspicion of atypical pneumonia (mycoplasma), for age > 5yr add azithromycin (**AAP Guideline**)
 - Influenza antiviral therapy should be administered as soon as possible to children with moderate to severe CAP consistent with influenza virus infection. Influenza treatment if clinical or laboratory diagnosis per current CDC recommendations (**Strong Recommendation; Moderate Quality Evidence**)
 - Outpatient/Inpatient
 - Moderate
 - Initiate parenteral antibiotic therapy: Ampicillin 150-200 mg/kg/day divided q 6 hrs – max dose 4 g/day; see footnote for children with penicillin allergy and/or underimmunized children (AAP Guideline)
 - If suspicion of atypical pneumonia (mycoplasma), for age > 5yr add azithromycin (AAP Guideline)
 - Influenza treatment if clinical or laboratory diagnosis per current CDC recommendations (**Strong Recommendation; Moderate Quality Evidence**)
 - Severe
 - Ampicillin or penicillin G should be administered to the fully immunized infant or school-age child admitted to a hospital ward with CAP (**Strong Recommendation; Moderate Quality Evidence**)
 - For patients who are not fully immunized, empiric therapy with a third-generation parenteral cephalosporin (ceftriaxone or cefotaxime) should be prescribed) (**Conditional Recommendation; Moderate Quality Evidence – IDSA Guideline**)
 - Empiric combination therapy with a macrolide (oral or parenteral), in addition to a b-lactam antibiotic, should be prescribed for the hospitalized child for whom M. pneumoniae and C. pneumoniae are significant considerations (**Strong Recommendation; Moderate Quality Evidence – IDSA Guideline**)
 - If suspicion of atypical pneumonia (mycoplasma), for age > 5yr add azithromycin (AAP Guideline)

- Influenza treatment if clinical or laboratory diagnosis per current CDC recommendations (**Strong Recommendation; Moderate Quality Evidence**)

Additional considerations:

- When other viruses are detected in a nasopharyngeal sample and/or the chest radiograph is most compatible with viral pneumonia (ie, without consolidations), manage with supportive care (ie, oxygen and rehydration if required) without antibiotics, unless there is convincing evidence of a secondary bacterial pneumonia. (Canadian Guidelines)
- If influenza is detected or suspected, strong consideration should be given to prompt treatment with neuraminidase inhibitors (oseltamivir, zanamivir).
- If penicillin allergy, administer cephalosporin (oral cefpodoxime, cefuroxime, or cefprozil; parenteral ceftriaxone or cefotaxime)
 - If severe penicillin allergy: oral levofloxacin (16-20 mg/kg/day divided q 12 hr (age 6 mos- 5 yrs) or 8-10 mg/kg/day (age 5-16 yrs) once daily (max daily dose 750 mg); clindamycin (40 mg/kg/day divided q 8 hr- max dose 600 mg), or linezolid
- In underimmunized children: oral amoxicillin-clavulanate or parenteral 3rd generation cephalosporin (ceftriaxone, cefotaxime)
- Children who experience respiratory failure or septic shock associated with pneumonia should receive empiric therapy with a third generation cephalosporin because it offers broader coverage.
- Additional recommendations for inpatient treatment:
 - Analgesia can be given to relieve discomfort from fever or pain related to the Pneumonia
 - Oxygen should be provided to patients to keep their saturations equal to or above 95%
 - When oxygen therapy required, consider warm, humidified oxygen (if available)
 - Patients exclusively on intravenous fluids require daily monitoring of their electrolytes to monitor for syndrome of inappropriate antidiuretic hormone (SIADH) 20
 - Chest physiotherapy has not been shown to be beneficial and is not recommended 20
 - In any progressively unwell child, consideration should be given to transfer the patient to a higher care facility.
 - For patients with signs/symptoms or blood gas concerning for impending respiratory failure, provide respiratory support as needed; supplemental oxygen to maintain oxygen saturations >90%
 - Maintain circulatory status/manage shock if present

Limitations for consideration

- Populations ages varied in guidelines and primary literature, may consider different treatment options for different age groups
- Limited data for macrolides

External Guidelines

In 2011, the **Pediatric Infectious Diseases Society and the Infectious Diseases Society of American (IDSA)** recommended the following:

Outpatients

- Antimicrobial therapy is not routinely required for preschool-aged children with CAP, because viral pathogens are responsible for the great majority of clinical disease. **(strong recommendation; high-quality evidence)**
- Amoxicillin should be used as first-line therapy for previously healthy, appropriately immunized infants and preschool children with mild to moderate CAP suspected to be of bacterial origin. Amoxicillin provides appropriate coverage for *Streptococcus pneumoniae*, the most prominent invasive bacterial pathogen. Table 5 lists preferred agents and alternative agents for children allergic to amoxicillin. **(strong recommendation; moderate-quality evidence)**
- Amoxicillin should be used as first-line therapy for previously healthy appropriately immunized school-aged children and adolescents with mild to moderate CAP for *S. pneumoniae*, the most prominent invasive bacterial pathogen. Atypical bacterial pathogens (eg, *M. pneumoniae*), and less common lower respiratory tract bacterial pathogens, as discussed in the Evidence Summary, should also be considered in management decisions. **(strong recommendation; moderate-quality evidence)**
- Macrolide antibiotics should be prescribed for treatment of children (primarily school-aged children and adolescents) evaluated in an outpatient setting with findings compatible with CAP caused by atypical pathogens. Laboratory testing for *M. pneumoniae* should be performed if available in a clinically relevant time frame. Table 5 lists preferred and alternative agents for atypical pathogens. **(weak recommendation; moderate-quality evidence)**
- Influenza antiviral therapy (Table 6) should be administered as soon as possible to children with moderate to severe CAP consistent with influenza virus infection during widespread local circulation of influenza viruses, particularly for those with clinically worsening disease documented at the time of an outpatient visit. Because early antiviral treatment has been shown to provide maximal benefit, treatment should not be delayed until confirmation of positive influenza test results. Negative results of influenza diagnostic tests, especially rapid antigen tests, do not conclusively exclude influenza disease. Treatment after 48 hours of symptomatic infection may still provide clinical benefit to those with more severe disease. **(strong recommendation; moderate-quality evidence)**

Inpatients

- Ampicillin or penicillin G should be administered to the fully immunized infant or school-aged child admitted to a hospital ward with CAP when local epidemiologic data document lack of substantial high-level penicillin resistance for invasive *S. pneumoniae*. Other antimicrobial agents for empiric therapy are provided in Table 7. **(strong recommendation; moderate-quality evidence)**
- Empiric therapy with a third-generation parenteral cephalosporin (ceftriaxone or cefotaxime) should be prescribed for hospitalized infants and children who are not fully immunized, in

regions where local epidemiology of invasive pneumococcal strains documents high-level penicillin resistance, or for infants and children with life-threatening infection, including those with empyema (Table 7). Non- β -lactam agents, such as vancomycin, have not been shown to be more effective than third-generation cephalosporins in the treatment of pneumococcal pneumonia for the degree of resistance noted currently in North America. **(weak recommendation; moderate-quality evidence)**

- Empiric combination therapy with a macrolide (oral or parenteral), in addition to a β -lactam antibiotic, should be prescribed for the hospitalized child for whom *M. pneumoniae* and *C. pneumoniae* are significant considerations; diagnostic testing should be performed if available in a clinically relevant time frame (Table 7). **(weak recommendation; moderate-quality evidence)**
- Vancomycin or clindamycin (based on local susceptibility data) should be provided in addition to β -lactam therapy if clinical, laboratory, or imaging characteristics are consistent with infection caused by *S. aureus* (Table 7). **(strong recommendation; low-quality evidence)**

How Can Resistance to Antimicrobials Be Minimized?

- Antibiotic exposure selects for antibiotic resistance; therefore, limiting exposure to any antibiotic, whenever possible, is preferred. **(strong recommendation; moderate-quality evidence)**
- Limiting the spectrum of activity of antimicrobials to that specifically required to treat the identified pathogen is preferred. **(strong recommendation; low-quality evidence)**
- Using the proper dosage of antimicrobial to be able to achieve a minimal effective concentration at the site of infection is important to decrease the development of resistance. **(strong recommendation; low-quality evidence)**
- Treatment for the shortest effective duration will minimize exposure of both pathogens and normal microbiota to antimicrobials and minimize the selection for resistance. **(strong recommendation; low-quality evidence)**

In 2018, the **Canadian Paediatric Society** recommended the following:

- If influenza is detected or suspected, strong consideration should be given to prompt treatment with neuraminidase inhibitors (oseltamivir, zanamivir).
- When other viruses are detected in a nasopharyngeal sample and/or the chest radiograph is most compatible with viral pneumonia (ie, without consolidations), manage with supportive care (ie, oxygen and rehydration if required) without antibiotics, unless there is convincing evidence of a secondary bacterial pneumonia.
- Outpatients with lobar or broncho-pneumonia should usually be treated with oral amoxicillin.
- Patients who require hospitalization but do not have a life-threatening illness should usually be started empirically on intravenous ampicillin. There is recent data demonstrating that ampicillin alone leads to a good clinical outcome in almost all cases of community-acquired pneumonia, including cases that require hospitalization.
- Children who experience respiratory failure or septic shock associated with pneumonia should receive empiric therapy with a third generation cephalosporin because it offers broader coverage. Ceftriaxone or cefotaxime offer better coverage than amoxicillin or ampicillin for



beta-lactamase-producing H influenzae and may be more efficacious against high-level penicillin-resistant pneumococcus – and possibly provide empirical coverage for the rare methicillin-susceptible S aureus (a rare cause of pneumonia). However, when there is rapidly progressing multilobar disease or pneumatoceles, the addition of vancomycin is suggested empirically to provide extra coverage for MRSA until culture results are available. If results of microbiological investigations in these patients do not reveal a pathogen, transitioning to ampicillin with subsequent oral amoxicillin is reasonable.

In 2018, **New South Wales** recommended the following:

Outpatient management

- Analgesia can be given to relieve discomfort from fever or pain related to the pneumonia
- Follow-up should be arranged to evaluate the patient for any deterioration.

Inpatient management

- Analgesia can be given to relieve discomfort from fever or pain related to the Pneumonia
- Oxygen should be provided to patients to keep their saturations equal to or above 95%
- When oxygen therapy required, consider warm, humidified oxygen (if available)
- Patients exclusively on intravenous fluids require daily monitoring of their electrolytes to monitor for syndrome of inappropriate antidiuretic hormone (SIADH) 20
- Chest physiotherapy has not been shown to be beneficial and is not recommended 20
- In any progressively unwell child, consideration should be given to transfer the patient to a higher care facility.

In 2017 the **American Academy of Pediatrics Section on Emergency Medicine Committee on Quality Transformation** recommended the following:

Mild

- Initiate oral antibiotic therapy: Amoxicillin 90 mg/kg/day divided TID (max dose 3 g/day), see footnote for children with penicillin allergy and/or underimmunized children
- Alternate dosing regimen of 90 mg/kg/day divided BID may be acceptable if lower rates of pneumococcal resistance (consider local resistance patterns and MICs)
- Duration of therapy: 7-10 days
- If suspicion of atypical pneumonia (mycoplasma), for age > 5yr add azithromycin
- Influenza treatment if clinical or laboratory diagnosis per current CDC recommendations

Moderate

- Initiate parenteral antibiotic therapy: Ampicillin 150-200 mg/kg/day divided q 6 hrs – max dose 4 g/day; see footnote for children with penicillin allergy and/or underimmunized children
- If suspicion of atypical pneumonia (mycoplasma), for age > 5yr add azithromycin
- Influenza treatment if clinical or laboratory diagnosis per current CDC recommendations

Severe

- Initiate parenteral antibiotic therapy:
 - Ceftriaxone: 100 mg/kg/day divided q 12-24 hrs

OR

- Cefotaxime: 150 mg/kg/day divided q 8 hrs⁴
- If Staph aureus suspected (multifocal pneumonia, necrotizing pneumonia/cavitary lesion, leukopenia):
 - Vancomycin: 40-60 mg/kg/day divided q 6-8 hrs

OR

- Clindamycin: 40 mg/kg/d divided q 6-8 hrs
- If suspicion of atypical pneumonia (mycoplasma), for age > 5yr add azithromycin
- For patients with signs/symptoms or blood gas concerning for impending respiratory failure, provide respiratory support as needed; supplemental oxygen to maintain oxygen saturations >90%
- Maintain circulatory status/manage shock if present
- Influenza treatment if clinical or laboratory diagnosis per current CDC recommendations

Footnotes:

- If penicillin allergy, administer cephalosporin (oral cefpodoxime, cefuroxime, or cefprozil; parenteral ceftriaxone or cefotaxime)
 - If severe penicillin allergy: oral levofloxacin (16-20 mg/kg/day divided q 12 hr (age 6 mos- 5 yrs) or 8-10 mg/kg/day (age 5-16 yrs) once daily (max daily dose 750 mg); clindamycin (40 mg/kg/day divided q 8 hr- max dose 600 mg), or linezolid
- In underimmunized children: oral amoxicillin-clavulanate or parenteral 3rd generation cephalosporin (ceftriaxone, cefotaxime)
- Effusion > 10 mm rim or >1/4 hemi-thorax opacified
- If severe penicillin allergy: Levofloxacin OR Clindamycin Or Linezolid
- Azithromycin: IV--10 mg/kg (max dose 500 mg) day 1 and 2, then transition to oral; Oral--10 mg/kg (max dose 500 mg) once on day 1, then 5 mg/kg (max dose 250 mg) once daily on days 2-5

In 2012, the **American Academy of Family Physicians** recommended:

SORT: KEY RECOMMENDATIONS FOR PRACTICE		
<i>Clinical recommendation</i>	<i>Evidence rating</i>	<i>References</i>
The absence of tachypnea is the most useful clinical finding for ruling out CAP in children.	C	1, 15, 16
Chest radiography has not been shown to improve clinical outcomes or change treatment of CAP in children.	B	17
Empiric antibiotic choices in children with CAP should be based on the patient's age and severity of illness, and local resistance patterns of pathogens.	C	7, 25, 26
Oral amoxicillin and intravenous penicillin G are equally effective in the treatment of hospitalized children with nonsevere CAP. However, amoxicillin is generally more cost-effective.	B	27
Macrolides are the empiric antibiotics of choice for children five to 16 years of age with CAP because of their activity against <i>Mycoplasma pneumoniae</i> and <i>Chlamydia pneumoniae</i> .	C	7, 25, 26
Routine childhood immunization with the pneumococcal conjugate vaccine significantly reduces the incidence of invasive pneumococcal disease in children.	A	8, 36, 37

CAP = community-acquired pneumonia.

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to <http://www.aafp.org/afpsort.xml>.

Mathur, 2018 included a comparison of international guidance for antibiotic therapy

Guideline	Last update	Recommendation
British National Formulary for Children (BNFc) [8]	2016	<ul style="list-style-type: none"> • Benzylpenicillin with gentamicin for neonatal sepsis of all causes • For children aged 1 month to 18 years, oral amoxicillin is recommended as first-line for CAP and clarithromycin is recommended if there is no response to treatment • For suspected staphylococcal infection, oral amoxicillin and flucloxacillin or amoxicillin clavulanate alone are recommended. • In complicated pneumonia or if oral administration is not possible, treatment for 7 days with intravenous amoxicillin or amoxicillin clavulanate or cefuroxime or cefotaxime is recommended. • For children aged 1 month–18 years who are allergic to penicillin, clarithromycin for 7 days is recommended
RCPCH/ESPID Manual of Childhood Infections, 'Blue Book' [9]	2016	<ul style="list-style-type: none"> • For children aged <5 years, oral amoxicillin for a standard course of 5 days is the first-choice antibiotic. • Macrolides are recommended if either <i>M. pneumoniae</i> or <i>Chlamydia pneumoniae</i> is suspected. • Intravenous antibiotics for severe pneumonia include penicillin/amoxicillin, amoxicillin clavulanate, cefuroxime and cefotaxime/ceftriaxone
British Thoracic Society [7]	2011	<ul style="list-style-type: none"> • Amoxicillin is first choice for oral antibiotic therapy in all children because it is effective against the majority of pathogens, is well tolerated and is cheap • Alternatives are amoxicillin clavulanate, cefaclor, erythromycin, azithromycin and clarithromycin • Macrolide antibiotics may be added at any age if there is no response to first-line empirical therapy • Macrolide antibiotics should be used if either mycoplasma or <i>C. pneumoniae</i> is suspected or in very severe disease. • Amoxicillin clavulanate is recommended for pneumonia associated with influenza
Canadian Paediatric Society [11]	2015	<ul style="list-style-type: none"> • Oral amoxicillin is recommended for outpatients with lobar or broncho-pneumonia. • Patients who require hospitalisation but do not have a life-threatening illness should be commenced empirically on intravenous ampicillin. • Empirical therapy with a third-generation cephalosporin is recommended for children who experience respiratory failure or septic shock associated with pneumonia. • Ceftriaxone or cefotaxime are recommended for β-lactamase-producing <i>H. influenzae</i> and high-level penicillin-resistant pneumococcus. • For rapidly progressing multilobar disease or pneumatoceles, the addition of vancomycin is suggested empirically with de-escalation to ampicillin with subsequent oral amoxicillin. • Vancomycin is recommended for empyema owing to <i>S. aureus</i>. • If <i>S. pneumoniae</i> is detected in blood or respiratory secretions and is penicillin-susceptible, treatment with either intravenous ampicillin or penicillin is recommended, followed by oral therapy with amoxicillin. • Treatment of <i>M. pneumoniae</i> and <i>C. pneumoniae</i> is azithromycin for 5 days. Doxycycline for children aged ≥8 years
ESPID [10]	2012	<ul style="list-style-type: none"> • For children <1 month, ampicillin/amoxicillin and gentamicin are recommended empirically. If <i>Listeria monocytogenes</i> or <i>enterococcus</i> is suspected, ampicillin with an alternative of a cephalosporin is recommended. Third-generation cephalosporins should be avoided in neonates because of the risk of candidiasis. For critically ill patients, an anti-staphylococcal penicillin and clindamycin or vancomycin are recommended. • For children aged 1–3 months, β-lactam antibiotics with anti-staphylococcal penicillin for the critically ill are recommended. In children with no fever or severe cough, <i>C. trachomatis</i> and <i>Bordetella pertussis</i> should be suspected and treated with macrolides. • For children aged 3 months to 5 years, penicillin G or aminopenicillins, e.g. amoxicillins are recommended to ensure adequate cover of <i>S. pneumoniae</i> and more atypical pathogens in this age group. For unimmunised children, treatment with amoxicillin clavulanate or a third-generation cephalosporin is recommended. Second-generation cephalosporins may be used in areas of low penicillin resistance. • For atypical pathogens, combined therapy with β-lactams (e.g. amoxicillin clavulanate) and macrolides (e.g. clarithromycin) are recommended as well as anti-staphylococcal antibiotics for the critically ill
IDSA/PIDS [12]	2011	<ul style="list-style-type: none"> • For children under 5 years of age, the guidelines recommend amoxicillin, amoxicillin clavulanate for presumed bacterial pneumonia and macrolides (azithromycin, clarithromycin or erythromycin) for presumed atypical pathogens. • For children over 5 years of age, amoxicillin, amoxicillin clavulanate and a macrolide can be added. The IDSA/PIDS guidelines recommend doxycycline for children >7 years

Primary literature

Source, Year	Study (N)	Summary of findings	Quality
Lodha, 2013	Systematic Review (N=3,952)	Non-severe CAP: Amoxicillin compared with cotrimoxazole had similar failure rates (odds ratio (OR) 1.18, 95% confidence interval (CI)	Low to unclear risk of bias

		<p>0.91 to 1.51) and cure rates (OR 1.03, 95% CI 0.56 to 1.89).</p> <p>In children presenting with CAP without underlying illness, and where point of care tests for identification of etiological agents for pneumonia are not available, empirical antibiotics may be used as follows.</p> <p>For the treatment of WHO-defined non-severe community-acquired pneumonia (CAP) in children below five years of age amoxicillin is an alternative to co-trimoxazole. There are no apparent differences between azithromycin and erythromycin, azithromycin and coamoxyclavulanic acid, or cefpodoxime and co-amoxyclavulanic acid. There are limited data on other antibiotics: co-amoxyclavulanic acid and cefpodoxime may be alternative second-line drugs.</p>	
<p>Lodha, 2013</p>	<p>Systematic Review (N=4,331)</p>	<p>Severe pneumonia without hypoxemia: oral antibiotics (amoxicillin/co-trimoxazole) compared with injectable penicillin had similar failure rates (OR 0.84, 95% CI 0.56 to 1.24), hospitalization rates (OR 1.13, 95% CI 0.38 to 3.34) and relapse rates (OR 1.28, 95% CI 0.34 to 4.82).</p>	<p>Low to unclear risk of bias</p>



		<p>In children presenting with CAP without underlying illness, and where point of care tests for identification of etiological agents for pneumonia are not available, empirical antibiotics may be used as follows.</p> <p>Severe pneumonia in children below five years of age, without hypoxia and accepting oral feeds, can be managed with oral amoxicillin on an ambulatory basis.</p>	
Lodha, 2016	Systematic Review (4 RCTs, N=4,400)	<p>Failure rate in children receiving oral antibiotics was 13% (288/2208) while that in children receiving parenteral antibiotics was 13.8% (302/2183)</p> <ul style="list-style-type: none"> • OR 0.93; 95% CI 0.78, 1.11 	Low to unclear risk of bias
Biondi, 2014	Systematic Review (17 trials)	<p>Spectrum vs. nonspectrum treatment of <i>M. pneumoniae</i> in children suggested pooled risk difference of 0.12 (95% CI, -.04 to 0.20)</p> <p><i>C. pneumoniae</i> and <i>M. pneumoniae</i> responded equally to treatment. Data suggests that 12% of children treated with a macrolide will have more rapid clinical improvement, corresponding to a number needed to treat of 8.33, but the confidence interval overlapping 0% negates statistical significance.</p>	High risk of bias

<p>Lodha, 2018</p>	<p>Systematic Review (N=1,116)</p>	<p>Severe CAP: Death rates were higher in children receiving chloramphenicol compared to those receiving penicillin/ampicillin plus gentamicin (OR 1.25, 95% CI 0.76 to 2.07).</p> <p>In children presenting with CAP without underlying illness, and where point of care tests for identification of etiological agents for pneumonia are not available, empirical antibiotics may be used as follows.</p> <p>For children below five years of age, hospitalized with severe and very severe CAP, penicillin/ampicillin plus gentamycin is superior to chloramphenicol. Other alternatives may be co-amoxiclavulanic acid, ceftriaxone, levofloxacin and cefuroxime.</p>	<p>Low to unclear risk of bias</p>
<p>Dinur-Schejter, 2012</p>	<p>Retrospective chart review (N=319)</p>	<p>Treatment failure was not significantly different (7.6% vs. 4.7%)</p> <p>Number of days of IV treatment, days of oxygen requirement, and days of hospitalization were similar (2.36 +/- 1.6 days vs. 2.59 +/- 1.6 days, 0.31 +/- 1.2 days vs. 0.64 +/- 1.3 days, and 2.67 +/- 1.4 days vs. 2.96 +/- 1.7 days, respectively).</p> <p>The number of patients who were febrile or required oxygen 72 hr after admission was similar (13.0% vs. 16.5%)</p>	<p>Moderate risk of bias</p>

		and 8.7% vs. 20.9%, respectively). One week after admission no difference between the two groups was seen	
Amarilyo, G, 2014	RCT (N=58, aged 3 months to 15 years)	The children in all arms (low-dose penicillin G, high penicillin G, and cefuroxime) recovered at the same rate with no significant difference Days of fever before admission (mean +/- SD) Low-dose 2.53 +/- 1.83 High-dose 2.59 +/- 1.71 Cefuroxime 2.79 +/- 1.04 p=0.99 Rectal temperature in Celsius (mean +/- SD) Low-dose 38.7 +/- 1.1 High-dose 38.8 +/- 0.9 Cefuroxime 38.9 +/- 1.0 p=0.75 Leukocyte count (x10 ³ /mL) Low-dose 23.9 +/- 10 High-dose 26.6 +/- 13.6 Cefuroxime 23.1 +/- 12.2 p=0.52	Moderate risk of bias

Quality of evidence (GRADE)

Quality of evidence (GRADE) –Amoxicillin

Risk of bias	Imprecision	Inconsistency	Indirectness	Publication bias	Certainty (Overall)
Low to unclear	Precise	Consistent	Direct	No	Moderate

Certainty: Moderate suggests future research will likely have an important impact on confidence in the estimate of effect and may change the estimate.

Quality of evidence (GRADE) – Oral Antibiotics

Risk of bias	Imprecision	Inconsistency	Indirectness	Publication bias	Certainty (Overall)
Low to unclear	Precise	Consistent	Direct	No	Moderate

Note: Moderate suggests future research will likely have an important impact on confidence in the estimate of effect and may change the estimate.



Quality of evidence (GRADE) – Macrolides

Risk of bias	Imprecision	Inconsistency	Indirectness	Publication bias	Certainty (Overall)
High	Precise	Inconsistent	Direct	Yes	Low

Note: Moderate suggests future research will likely have an important impact on confidence in the estimate of effect and may change the estimate.

Quality of evidence (GRADE) – Penicillin/ampicillin

Risk of bias	Imprecision	Inconsistency	Indirectness	Publication bias	Certainty (Overall)
Low	Precise	Consistent	Direct	No	Moderate

Note: Moderate suggests future research will likely have an important impact on confidence in the estimate of effect and may change the estimate.

Quality of evidence (GRADE) – Broad spectrum

Risk of bias	Imprecision	Inconsistency	Indirectness	Publication bias	Certainty (Overall)
Moderate	Imprecise	Unknown	Direct	No	Low

Note: Low suggests future research will have an important impact on confidence in the estimate of effect and will likely change the estimate.

Question 4: What is the appropriate duration of antimicrobial therapy for CAP?

General consensus from literature and external guidelines

- Mild:
 - Initiate oral antibiotic therapy: Amoxicillin 90 mg/kg/day divided TID (max dose 3 g/day) for 7 to 10 days **(Consensus)**
 - Alternate dosing regimen of 90 mg/kg/day divided BID may be acceptable if lower rates of pneumococcal resistance (consider local resistance patterns and MICs)
 - Duration of therapy: 7-10 days
- Moderate
 - Outpatient: Amoxicillin 90 mg/kg/day **(Consensus)**
 - Inpatient: Initiate parenteral antibiotic therapy: Ampicillin 150-200 mg/kg/day divided q 6 hrs – max dose 4 g/day **(Consensus)**
- Severe
 - Initiate parenteral antibiotic therapy: **(Consensus)**
 - Ceftriaxone: 100 mg/kg/day divided q 12-24 hrs, or:
 - Cefotaxime: 150 mg/kg/day divided q 8 hrs⁴
 - If Staph aureus suspected (multifocal pneumonia, necrotizing pneumonia/cavitary lesion, leukopenia): **(Consensus)**
 - Vancomycin: 40-60 mg/kg/day divided q 6-8 hrs, or:
 - Clindamycin: 40 mg/kg/d divided q 6-8 hrs
- Penicillin Allergy **(Consensus)**
 - If severe penicillin allergy: oral levofloxacin (16-20 mg/kg/day divided q 12 hr (age 6 mos- 5 yrs) or 8-10 mg/kg/day (age 5-16 yrs) once daily (max daily dose 750 mg); clindamycin (40 mg/kg/day divided q 8 hr- max dose 600 mg), or linezolid; Azithromycin Day 1: 10 mg per kg, Day 2 through 5: 5 mg per kg per day
- Other considerations
 - Treatment courses of 10 days have been best studied, although shorter courses may be just as effective, particularly for more mild disease managed on an outpatient basis **(Strong Recommendation; Moderate Quality Evidence)**
 - Infections caused by certain pathogens, notably CAMRSA, may require longer treatment than those caused by *S. pneumoniae* **(Strong Recommendation; Moderate Quality Evidence)**

Limitations for consideration

- Limited studies on short-term duration

External Guidelines

In 2011, the **Pediatric Infectious Diseases Society and the Infectious Diseases Society of American (IDSA)** recommended the following:

- Treatment courses of 10 days have been best studied, although shorter courses may be just as effective, particularly for more mild disease managed on an outpatient basis. **(strong recommendation; moderate-quality evidence)**
- Infections caused by certain pathogens, notably CAMRSA, may require longer treatment than those caused by *S. pneumoniae*. **(strong recommendation; moderate-quality evidence)**

In 2018, the **Canadian Paediatric Society** recommended the following:

TABLE 2		
Doses of common antimicrobials recommended for suspected or proven bacterial pneumonia		
Antibiotic	Route	Regimen
Amoxicillin, maximum 4000 mg/day	PO	40–90 mg/kg/day divided 3 times daily*
Ampicillin, maximum 12 g/day	IV	200 mg/kg/day divided every 6 h
Ceftriaxone, maximum 4 g/day	IV	50–100 mg/kg/day divided every 12 h or 24 h
Cefotaxime	IV	150–200 mg/kg/day divided every 6 h to 8 h
Penicillin G (if confirmed to be due to <i>Streptococcus pneumoniae</i> that is penicillin-susceptible)	IV	200,000–250,000 U/day divided every 4 h to 6 h; maximum 24 million U/day
Azithromycin (for suspected or proven <i>Mycoplasma</i> or <i>Chlamydia</i> pneumoniae)	IV/PO	Given as a single daily dose; 10 mg/kg on day 1; 5 mg/kg on days 2 to 5; (5 days total) maximum 500 mg/day
Clarithromycin (for suspected or proven <i>Mycoplasma</i> or <i>Chlamydia</i> pneumoniae)	PO	15 mg/kg/day divided 2 times daily for 7 days

*Although twice-daily dosing is adequate for otitis media, three times-daily dosing is recommended for pneumonia. IV Intravenously; PO Orally

In 2018, **New South Wales** recommended the following:

9.1 Term neonates: ≤ 1 month of age

ALL NEONATES REQUIRE ADMISSION FOR INPATIENT MANAGEMENT - MILD, MODERATE OR SEVERE	
<p>Up to 7 days of age²¹ BENZYL PENICILLIN (Penicillin G) 50 mg/kg IV 12-hourly (max 300 mg/dose)</p> <p>Plus GENTAMICIN 4 mg/kg IV once daily (max 24 mg/dose)</p>	<p>8 to 28 days of age²¹ BENZYL PENICILLIN (Penicillin G) 50 mg/kg IV 6-hourly (max 300 mg/dose)</p> <p>Plus GENTAMICIN 4 mg/kg IV once daily (max 24 mg/dose)</p>
<p>NOTE: Herpes simplex virus pneumonitis may present between days 3 and 7 and requires expert advice regarding management.²¹ Consider:</p> <p>ACICLOVIR 20 mg/kg IV 8-hourly if risk factors for HSV pneumonitis</p> <p>Consider adding the following treatment for Chlamydia trachomatis*: AZITHROMYCIN 20 mg/kg orally daily for 3 days²² (max 120 mg/dose) or CLARITHROMYCIN 7.5 mg/kg orally 12-hourly for 7 days</p> <p>Consider adding the following for Bordetella pertussis*: AZITHROMYCIN 10 mg/kg orally daily for 5 days (max 50 mg/dose) or CLARITHROMYCIN 7.5 mg/kg orally 12-hourly for 7 days (max 37.5 mg/dose)</p> <p><i>Beware of atypical presentations e.g. apnoea.</i></p>	

*Azithromycin is the only drug recommended for *Bordetella pertussis* treatment or prophylaxis or treatment of *Chlamydia trachomatis* in children <1 month of age, it is associated with infantile hypertrophic pyloric stenosis, especially in babies <2 weeks old, though the benefit of using azithromycin outweighs this risk.

9.3 Infants and children: 4 months to 16 years

OUTPATIENT MANAGEMENT	INPATIENT MANAGEMENT	
MILD	MILD and MODERATE	SEVERE - seek expert advice as per local CERS and commence:
<p>AMOXICILLIN (amoxycillin)²¹ 25 mg/kg orally 8 hourly (max 1 g/dose)</p> <p>or If <i>Mycoplasma pneumoniae</i> suspected: CLARITHROMYCIN 7.5 mg/kg orally 12 hourly for 5 days (max 500 mg/dose) or AZITHROMYCIN 10 mg/kg orally daily for 5 days (max 500 mg/dose)</p> <ul style="list-style-type: none"> If no response to treatment review diagnosis, adherence to treatment and if there is a need for admission If infant/child is not tolerating oral therapy, then intravenous therapy (and hence admission) is required <p>PENICILLIN ALLERGY: Where Penicillin allergy exists use AZITHROMYCIN. See Section 11.</p>	<p>AMOXICILLIN (amoxycillin)²¹ 25 mg/kg orally, 8 hourly (max 1 g/dose)</p> <ul style="list-style-type: none"> If oral therapy not tolerated (vomiting) treat with BENZYL PENICILLIN 50 mg/kg IV 6 hourly Cefotaxime or ceftriaxone may be required if not responding to penicillin alone Change to oral amoxicillin or amoxicillin with clavulanic acid (if Cefotaxime was required) when tolerated and patient clinically improved <p>If <i>Mycoplasma pneumoniae</i> or other atypical suspected add: CLARITHROMYCIN 7.5 mg/kg orally 12 hourly for 5 days (max 500 mg/dose) or AZITHROMYCIN 10 mg/kg orally daily for 5 days (max 500 mg/dose)</p>	<p>CEFOTAXIME²¹ 50 mg/kg IV 8 hourly (max 2 g/dose) or CEFTRIAXONE²¹ 50 mg/kg IV or IM ONCE daily (max 2 g/dose)</p> <p>Plus CLINDAMYCIN 10 mg/kg IV 8 hourly (max 450 mg/dose) or LINCOMYCIN 15 mg/kg IV 8 hourly (max 600 mg/dose)</p> <p>If intubated or septic, change clindamycin or lincomycin to: VANCOMYCIN 15 mg/kg IV 6-hourly (up to 750 mg/dose) REFER TO PAEDIATRIC SEPSIS PATHWAY</p> <p>Plus if <i>Mycoplasma pneumoniae</i> or another atypical pathogen is suspected AZITHROMYCIN 10 mg/kg (up to 500 mg) IV, daily</p>

* Both cefotaxime and ceftriaxone have activity against methicillin-sensitive *Staphylococcus aureus*. Clindamycin or Lincomycin are recommended for empiric cover for methicillin-resistant *Staphylococcus aureus*.²³

Viral pneumonia is most prominent in the 3 month to 5 year age group, however if a bacterial pneumonia is suspected, antibiotic therapy is required. For **Mild and Moderate pneumonia** requiring admission it is recommended that **oral AMOXICILLIN** be used as first line treatment for patients admitted to hospital with uncomplicated pneumonia. **Oral AMOXICILLIN** has been shown to be safe and effective for inpatient treatment of CAP and is recommended.^{8, 24}

10 SPECIFIC PATHOGENS

10.1 Staphylococcus aureus

Staphylococcus aureus is usually suspected rather than confirmed. The presence of pleural effusions, pneumatoceles or lung abscesses are more indicative of Staphylococcal disease. Infection tends to be severe and require admission for inpatient management.

For suspected *Staphylococcus aureus* pneumonia:

- There has recently been an increased incidence of community acquired MRSA
- Indigenous and Pacific Island children (and adults) tend to be at higher risk of Staphylococcal infections due to community acquired MRSA
- Severely ill patients with suspected Staphylococcal pneumonia should be treated for both MRSA and non-MRSA pneumonia with the following:

STAPHYLOCOCCUS AUREUS - INPATIENT MANAGEMENT
<p>CEFOTAXIME 50 mg/kg IV 8-hourly (max 2 g/dose) or CEFTRIAXONE 50 mg/kg IV or IM daily (max 2 g/dose) NOT RECOMMENDED FOR NEONATES (0- 28days old)</p> <p>Plus CLINDAMYCIN 10 mg/kg IV 8 hourly (max 450 mg/dose) or LINCOMYCIN 15 mg/kg IV 8 hourly (max 600 mg/dose) NOT RECOMMENDED FOR NEONATES (0- 28days old)</p> <p>If intubated or septic add VANCOMYCIN (child)15 mg/kg IV 6 hourly (up to 750 mg/dose) VANCOMYCIN (neonates)15 mg/kg 12 hourly if 0-7days then 8 hourly if 8-28 days</p> <ul style="list-style-type: none"> • Consultation with the Respiratory Team +/- Infectious Diseases Team should be considered • Severely ill patients with confirmed Staphylococcal pneumonia should be treated according to available antibiotic sensitivity results <p>See Section 11 for Penicillin allergy</p>

10.2 Pertussis

Admit all infants under 6 months with suspected pertussis and children with cyanosis or apnoea. Frequent observations and monitoring with pulse oximetry is essential. Intensive care may be needed for children with episodes of cyanosis or apnoea. Pertussis, suspected or confirmed at any age should be treated with the following ²³:

PERTUSSIS OUTPATIENT MANAGEMENT - only infants and children greater than 6 months of age	PERTUSSIS INPATIENT MANAGEMENT - all infants under 6 months of age require admission
<p>AZITHROMYCIN 10 mg/kg orally for the first dose only (max 500 mg/dose) then 5 mg/kg daily for next 4 days (max 250 mg/dose) or CLARITHROMYCIN 7.5mg/kg orally 12 hourly for 7 days (max 500 mg/dose) or TRIMETHOPRIM + SULFAMETHOXAZOLE 4 + 20 mg/kg orally 12 hourly for 7 days (max 160 + 800 mg/dose)</p>	<p>Under 1 month: AZITHROMYCIN 10 mg/kg orally or IV daily (max 50 mg/dose) for 5 days or CLARITHROMYCIN 7.5mg/kg orally 12 hourly for 7 days (max 37.5 mg/dose)</p> <p>Age 1 – 6 months: AZITHROMYCIN 10 mg/kg orally for the first dose only (max 80 mg/dose) followed by 5 mg/kg oral daily for next 4 days (max 40 mg/dose) or CLARITHROMYCIN 7.5 mg/kg orally 12 hourly for 7 days (max 60 mg/dose) or TRIMETHOPRIM + SULFAMETHOXAZOLE 4 + 20 mg/kg orally 12-hourly for 7 days (max 32 + 160 mg/dose)</p>

11 PENICILLIN ALLERGY

1. Child known to tolerate cephalosporins:

MILD to MODERATE	
3 months to 2 years	CEFUROXIME 10 mg/kg/dose oral 12 hourly (max 125 mg/dose)
2 years to 12 years	CEFUROXIME 15 mg/kg/dose oral 12 hourly (max 250 mg/dose)
Greater than 12 years	CEFUROXIME 250mg/dose oral 12 hourly (max 500 mg/dose)
If parenteral therapy is required:	
Greater than 1 month	CEFOTAXIME 50 mg/kg IV 8 hourly (max 2 g/dose) or CEFTRIAZONE 50 mg/kg IV daily (max 2 g/dose)

2. There is a 7% chance of cross-reaction of cephalosporin with penicillin. Non-beta-lactam alternatives are Erythromycin, Clarithromycin or if greater than 8 years of age consider Doxycycline:

MILD to MODERATE	
Greater than 28 days	ERYTHROMYCIN 10 mg/kg/dose oral 6 hourly (max 500 mg/dose) or
All ages	CLARITHROMYCIN 7.5 mg/kg/dose oral 12 hourly (max 500 mg/dose) or
8 years or greater	DOXYCYCLINE 2 mg/kg/dose oral 12 hourly (max 100 mg/dose)

Streptococcus Pneumoniae or *Staphylococcus aureus* may be resistant to these above agents.

SEVERE	
0 - 6 days	VANCOMYCIN 15 mg/kg/dose IV 12 hourly (max 90 mg/dose) plus CIPROFLOXACIN 10 mg/kg/dose IV 12 hourly (max 60 mg/dose)
7 to 28 days	VANCOMYCIN 15 mg/kg/dose IV 8 hourly (max 90 mg/dose) plus CIPROFLOXACIN 10 mg/kg/dose IV 12 hourly (max 60 mg/dose)
Greater than 28 days	VANCOMYCIN 15 mg/kg/dose IV 6 hourly (max 750 mg/dose) plus CIPROFLOXACIN 10 mg/kg/dose IV 12 hourly (max 400 mg/dose)

9.2 Infants: 1 to 3 months

ALL INFANTS 1-3 MONTHS REQUIRE ADMISSION FOR INPATIENT MANAGEMENT	
MILD to MODERATE	SEVERE - seek expert advice as per local CERS and commence:
<p>BENZYL PENICILLIN²¹ 50 mg/kg IV 6 hourly (max 400 mg/dose)</p> <p>Consider adding the following treatment if <i>Chlamydia trachomatis</i> or <i>Bordetella pertussis</i> are suspected, particularly in the patient who is afebrile, only mildly unwell and has the typical clinical features of pneumonia²¹:</p> <p><i>Chlamydia trachomatis</i> AZITHROMYCIN 20 mg/kg orally daily for 3 days (max 160 mg/dose)</p> <p><i>Bordetella pertussis</i> AZITHROMYCIN 10 mg/kg orally daily for 5 days (max 80 mg/daily) or CLARITHROMYCIN 7.5 mg/kg orally 12 hourly for 7 days (max 60 mg/dose) or TRIMETHOPRIM + SULFAMETHOXAZOLE 4 + 20 mg/kg orally 12 hourly for 7 days (max 32 + 160 mg/dose)</p>	<p>CEFOTAXIME²¹ 50 mg/kg IV 8 hourly (max 400 mg/dose) or CEFTRIAZONE[†] 50 mg/kg/dose IV or IM ONCE daily (max 400 mg/dose)</p> <p>Plus</p> <p>CLINDAMYCIN 10 mg/kg IV 8 hourly (max 80 mg/dose) or LINCOMYCIN 15 mg/kg IV 8 hourly (max 120 mg/dose)</p> <p>If intubated or septic, change clindamycin or lincomycin to: VANCOMYCIN 15 mg/kg IV 6 hourly (max 120 mg/dose)</p> <p>Consider adding the following treatment if <i>Chlamydia trachomatis</i> or <i>Bordetella pertussis</i> are suspected.</p> <p><i>Chlamydia trachomatis</i> AZITHROMYCIN 20 mg/kg orally daily for 3 days (max 160 mg/dose)</p> <p><i>Bordetella pertussis</i> (whooping cough) AZITHROMYCIN 10 mg/kg orally daily for 5 days (max 80 mg/dose) or CLARITHROMYCIN 7.5 mg/kg orally 12 hourly for 7 days (max 60 mg/dose) or TRIMETHOPRIM + SULFAMETHOXAZOLE 4 + 20 mg/kg orally 12 hourly for 7 days (max 32 + 160 mg/dose)</p>

In 2017 the **American Academy of Pediatrics Section on Emergency Medicine Committee on Quality Transformation** recommended the following:

Mild

- Initiate oral antibiotic therapy: Amoxicillin 90 mg/kg/day divided TID (max dose 3 g/day), see footnote for children with penicillin allergy and/or underimmunized children
- Alternate dosing regimen of 90 mg/kg/day divided BID may be acceptable if lower rates of pneumococcal resistance (consider local resistance patterns and MICs)
- Duration of therapy: 7-10 days
- If suspicion of atypical pneumonia (mycoplasma), for age > 5yr add azithromycin
- Influenza treatment if clinical or laboratory diagnosis per current CDC recommendations

Moderate

- Initiate parenteral antibiotic therapy: Ampicillin 150-200 mg/kg/day divided q 6 hrs – max dose 4 g/day; see footnote for children with penicillin allergy and/or underimmunized children
- If suspicion of atypical pneumonia (mycoplasma), for age > 5yr add azithromycin
- Influenza treatment if clinical or laboratory diagnosis per current CDC recommendations

Severe

- Initiate parenteral antibiotic therapy:
 - Ceftriaxone: 100 mg/kg/day divided q 12-24 hrs

OR

- Cefotaxime: 150 mg/kg/day divided q 8 hrs⁴
- If Staph aureus suspected (multifocal pneumonia, necrotizing pneumonia/cavitary lesion, leukopenia):
 - Vancomycin: 40-60 mg/kg/day divided q 6-8 hrs

OR

- Clindamycin: 40 mg/kg/d divided q 6-8 hrs
- If suspicion of atypical pneumonia (mycoplasma), for age > 5yr add azithromycin
- For patients with signs/symptoms or blood gas concerning for impending respiratory failure, provide respiratory support as needed; supplemental oxygen to maintain oxygen saturations >90%
- Maintain circulatory status/manage shock if present
- Influenza treatment if clinical or laboratory diagnosis per current CDC recommendations

Footnotes:

- If penicillin allergy, administer cephalosporin (oral cefpodoxime, cefuroxime, or cefprozil; parenteral ceftriaxone or cefotaxime)
 - If severe penicillin allergy: oral levofloxacin (16-20 mg/kg/day divided q 12 hr (age 6 mos- 5 yrs) or 8-10 mg/kg/day (age 5-16 yrs) once daily (max daily dose 750 mg); clindamycin (40 mg/kg/day divided q 8 hr- max dose 600 mg), or linezolid



- In underimmunized children: oral amoxicillin-clavulanate or parenteral 3rd generation cephalosporin (ceftriaxone, cefotaxime)
- Effusion > 10 mm rim or >1/4 hemi-thorax opacified
- If severe penicillin allergy: Levofloxacin OR Clindamycin Or Linezolid
- Azithromycin: IV--10 mg/kg (max dose 500 mg) day 1 and 2, then transition to oral; Oral--10 mg/kg (max dose 500 mg) once on day 1, then 5 mg/kg (max dose 250 mg) once daily on days 2-5

In 2012, the **American Academy of Family Physicians** recommended:

Table 3. Recommended Empiric Outpatient Treatment of Childhood Community-Acquired Pneumonia

Age	Alberta guideline ²⁵	Cincinnati guideline ⁷
60 days to 5 years*	<p>Preferred regimens</p> <p>Amoxicillin†</p> <p>40 mg per kg per day for 7 to 10 days</p> <p>or</p> <p>90 mg per kg per day, in three divided doses, for 7 to 10 days</p> <p>Alternative regimens for patients allergic to penicillin or beta-lactam antibiotics</p> <p>Azithromycin (Zithromax)</p> <p>Day 1: 10 mg per kg</p> <p>Days 2 through 5: 5 mg per kg per day</p> <p>Clarithromycin (Biaxin)</p> <p>15 mg per kg per day, in two divided doses, for 7 to 10 days</p> <p>Erythromycin</p> <p>40 mg per kg per day, in four divided doses, for 7 to 10 days</p>	<p>Amoxicillin</p> <p>80 to 90 mg per kg per day, in two divided doses, for 7 to 10 days</p> <p>Azithromycin</p> <p>Day 1: 10 mg per kg</p> <p>Days 2 through 5: 5 mg per kg per day</p> <p>Clarithromycin</p> <p>15 mg per kg per day, in two divided doses, for 7 to 10 days</p> <p>Cefprozil (Cefzil)</p> <p>30 mg per kg per day, in two divided doses, for 7 to 10 days</p> <p>Cefuroxime (Ceftin)</p> <p>30 mg per kg per day, in two divided doses, for 7 to 10 days</p> <p>Ceftriaxone (Rocephin)‡</p> <p>Single dose of 50 mg per kg, administered intramuscularly</p> <p>Azithromycin </p> <p>Day 1: 10 mg per kg</p> <p>Days 2 through 5: 5 mg per kg per day</p>
5 to 16 years	<p>Azithromycin§</p> <p>Day 1: 10 mg per kg</p> <p>Days 2 through 5: 5 mg per kg per day</p>	<p>Azithromycin </p> <p>Day 1: 10 mg per kg</p> <p>Days 2 through 5: 5 mg per kg per day</p>

*—Age range in Alberta guideline is three months to five years.
†—Higher dose for patients who attend child care or who received antibiotics in the previous three months.
‡—Clarithromycin or erythromycin may be used as an alternative for seven to 10 days. Doxycycline (4 mg per kg per day orally every 12 hours) may be used in children older than eight years who are allergic to macrolides.
§—Follow with oral antibiotic therapy.
||—Clarithromycin may also be used for seven to 10 days.
Information from references 7, 25, and 26.

Table 4. Recommended Empiric Inpatient Treatment of Childhood Community-Acquired Pneumonia

Age	Alberta guideline ²⁵	Cincinnati guideline ⁷
60 days to 5 years*	Cefuroxime (Zinacef) 150 mg per kg per day IV, in divided doses, given every 8 hours for 10 to 14 days	See Table 3
	In critically ill patients: Cefuroxime 150 mg per kg per day IV, in divided doses, given every 8 hours for 10 to 14 days <i>plus</i> Erythromycin 40 mg per kg per day IV or orally, in divided doses, given every 6 hours for 10 to 14 days <i>or</i> Cefotaxime (Claforan) 200 mg per kg per day IV, in divided doses, given every 8 hours for 10 to 14 days <i>plus</i> Cloxacillin (no longer available in the United States) 150 to 200 mg per kg per day IV, in divided doses, given every 6 hours for 10 to 14 days	Not applicable
5 to 16 years	Cefuroxime 150 mg per kg per day IV, in divided doses, given every 8 hours for 10 to 14 days <i>plus</i> Erythromycin 40 mg per kg per day IV or orally, in divided doses, given every 6 hours for 10 to 14 days <i>or</i> Azithromycin (Zithromax) Day 1: 10 mg per kg IV or orally Days 2 through 5: 5 to 10 mg per kg per day IV or orally	See Table 3

IV = intravenously.

*—Age range in Alberta guideline is three months to five years.
Information from references 7, 25, and 26.

Primary literature evidence (highest level of evidence)

Source, Year	Study (N)	Summary of findings	Quality
Greenberg, 2014	RCT (N=140)	No children failed the 5-day (0/56) nor the 10-day (0/42) course. Overall, 4/10 failed the 3-day course.	Low risk of bias

Primary Literature (lower levels of evidence)

Source, Year	Study (N)	Summary of findings	Quality
Lopez-Alcalde, 2018	Systematic Review (N=0)	No RCTs were found that compared short- and longer-courses of the same antibiotic for the treatment of adolescents and adult outpatients with CAP	Unclear risk of bias



Quality of evidence (GRADE) – Short- vs long-term duration

Risk of bias	Imprecision	Inconsistency	Indirectness	Publication bias	Certainty (Overall)
Moderate	Imprecise	Unknown	Direct	No	Very Low

Note: Very Low suggests that any estimate of effect is very uncertain.



Question 5: What is the appropriate method and duration of patient monitoring to confirm adequate anti-microbial response?

Consensus from limited evidence from guidelines

- Children on adequate therapy should demonstrate clinical and laboratory signs of improvement within 48–72 hours (**Strong Recommendation; Moderate Quality Evidence**)
- For children whose condition deteriorates after admission and initiation of antimicrobial therapy or who show no improvement within 48–72 hours, further investigation should be performed (**Strong Recommendation; Moderate Quality Evidence**)

Limitations for consideration

- Monitoring was infrequently mentioned in evidence

External Guidelines

In 2011, the **Pediatric Infectious Diseases Society and the Infectious Diseases Society of American (IDSA)** recommended the following:

- Children on adequate therapy should demonstrate clinical and laboratory signs of improvement within 48–72 hours. For children whose condition deteriorates after admission and initiation of antimicrobial therapy or who show no improvement within 48–72 hours, further investigation should be performed. (**strong recommendation; moderate-quality evidence**)

Health System Guidelines

The 2017 **Children’s Hospital of Philadelphia (CHOP)** Pathway for Evaluation and Treatment of Child with Community-Acquired Pneumonia stated:

- If increasing respiratory distress, increasing respiratory support requirement, or worsening fever curve after > 48 hours of preferred first line therapy, consider Treatment Failure.



Question 6: How should a parapneumonic effusion be identified?

Consensus from guidelines

- History and physical examination may be suggestive of parapneumonic effusion in children suspected of having CAP, but chest radiography should be used to confirm the presence of pleural fluid. If the chest radiograph is not conclusive, then further imaging with chest ultrasound or computed tomography (CT) is recommended. **Strong recommendation, moderate / high quality**

- Diagnosis of effusion:
 - + CXR (PA or AP upright and lateral)
 - If CXR inconclusive or >small effusion (10mm rim of fluid on lateral or opacity greater than ¼ thorax), chest ultrasound (preferred) or chest CT. **Strong recommendation, low quality**

Question 7: What factors are important in determining whether drainage of the parapneumonic effusion is required?

Consensus from guidelines

Main two factors: clinical and imaging (see next page for specifics)

- Size (strong, moderate)
- Respiratory compromise (strong, moderate)

May require drainage:

- Large and/or growing in size
- Impairing pulmonary function
- Organized and loculated
- Preventing adequate response to antibiotics

Surgical intervention is indicated when sepsis and infected fluid are not effectively controlled with antibiotics alone and/or in the presence of significant respiratory compromise.

- Free-flowing fluid: chest tube + fibrinolytics (tPA, qd for 3 days) within 24 hours or VATS within 48 hours after initiation of antibiotic therapy
- Empyema: VATS within 48 hours
- Small effusion (opacity less than $\frac{1}{4}$ of thorax, <10 mm rim of fluid on lateral)
 - Tx with antibiotics, **do not drain** or obtain fluid for culture
 - If no response to antibiotics, reassess size: if still small, continue antibiotics and do not drain; if moderate or large, follow large effusion algorithm
- Moderate effusion (opacity greater than $\frac{1}{4}$ but less than $\frac{1}{2}$ of thorax, >10 mm rim of fluid):
 - Consult with surgical or IR
 - if **mild** degree of respiratory compromise, tx with antibiotics and consider thoracentesis, can perform chest ultrasound or CT in conjunction with drainage. If worsens despite IV antibiotics, follow large effusion algorithm.
 - if **moderate to severe** degree of respiratory compromise, obtain pleural fluid for culture, drain space; can perform chest ultrasound or CT with drainage.
- Large effusion (opacity greater than $\frac{1}{2}$ of thorax)
 - Consult with surgical or IR
 - Obtain pleural fluid, drain space; can perform chest ultrasound or CT with drainage.
 - Consider primary video assisted thorascopic surgery.

Question 8. What laboratory testing should be performed on pleural fluid?

External Guidelines:

In 2011, the **Pediatric Infectious Diseases Society and the Infectious Diseases Society of American (IDSA)** recommended the following:

- Gram stain and bacterial culture of pleural fluid should be performed whenever a pleural fluid specimen is obtained. **(Strong Recommendation; High Quality Evidence)**
- Antigen testing or nuclei acid amplification through polymerase chain reaction (PCR) increase the detection of pathogens in pleural fluid and may be useful for management. **(Strong Recommendation; Moderate Quality Evidence)**
- Analysis of pleural fluid parameters such as pH and levels of glucose, protein, and lactate dehydrogenase, rarely change patient management and are not recommended. **(Weak Recommendation; Very Low Quality Evidence)**
- Analysis of the pleural fluid white blood cell (WBC) count, with cell differential analysis, is recommended primarily to help differentiate bacterial from mycobacterial etiologies and from malignancy. **(Weak Recommendation; Moderate Quality Evidence)**

The 2018 **Canadian Paediatric Society** stated the following:

- Ultrasound at the point of care appears to be sensitive and specific for detecting pneumonic infiltrates but requires further validation. Ultrasound and computed tomography are also useful in the diagnosis of complicated pneumonia. Both will detect parapneumonic effusions, which often accompany uncomplicated pneumonia, as well as empyemas, where persistent fever is a predominant symptom.

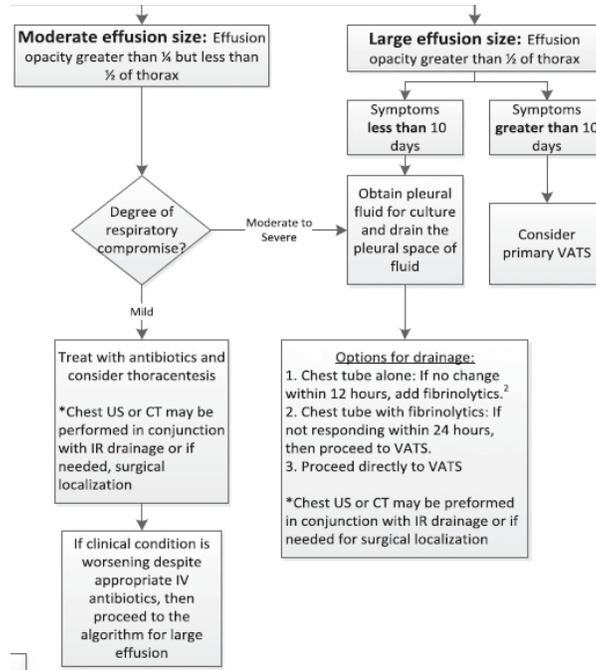
In 2018, **New South Wales** recommended the following:

- If the required expertise is available, pleural fluid may be aspirated for diagnostic purposes when there is evidence of an effusion present. However, in children it would be rare to perform this procedure due to its traumatic nature. Ultrasound guided thoracentesis is the accepted clinical standard in children as it reduces the risk for iatrogenic pneumothorax. A specimen should be sent for biology and virology. Culture positive rates are in the order of 17–20%.

In 2017, the **American Academy of Pediatrics** recommended the following:

- Moderate effusion size: Effusion opacity greater than $\frac{1}{4}$ but less than $\frac{1}{2}$ of thorax
 - Chest US or CT may be performed in conjunction with IR drainage or if needed, surgical localization
- Large effusion size: Effusion opacity greater than $\frac{1}{2}$ of thorax
 - Symptoms less than 10 days – Obtain pleural fluid for culture and drain the pleural space of fluid
 - Options for drainage:
 - Chest tube alone: If no change within 12 hours, add fibrinolytics

- Chest tube with fibrinolytics: If not responding within 24 hours, then process to VATS
- Chest US or CT may be performed in conjunction with IR drainage or if needed, surgical localization



In 2017 the **American Academy of Pediatrics Section on Emergency Medicine Committee on Quality Transformation** recommended the following:

- Use CXR to demonstrate moderate to large pleural effusions (Effusion > 10 mm rim or >1/4 hemi-thorax opacified)

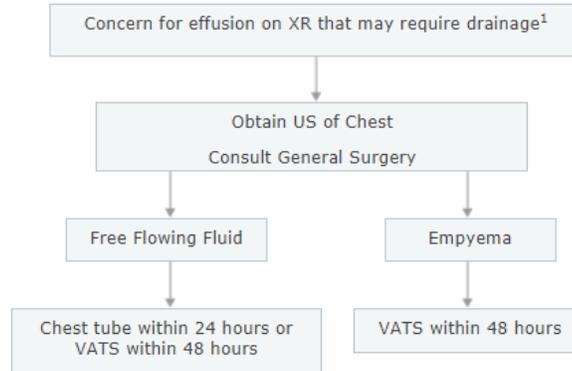
Health System Guidelines:

Children’s Hospital of Philadelphia (CHOP), 2017

- Evaluation and Management of Pleural Effusion
 - Concern for effusion on XR that may require drainage
 - Effusions that may require drainage are those that the clinician is concerned are:
 - Large and/or growing in size
 - Impairing pulmonary function
 - Organized and loculated
 - Preventing adequate response to antibiotics
 - Obtain US of Chest; General Surgery
 - Free flowing fluid
 - Chest tube within 24 hours or VATs within 48 hours
 - Empyema

- VATS within 48 hours

Evaluation and Management of Pleural Effusion



1. Effusions that may require drainage are those that the clinician is concerned are:

1. Large and/or growing in size
2. Impairing pulmonary function
3. Organized and loculated
4. Preventing adequate response to antibiotics

Children’s Hospital of Colorado, 2016 – Followed AAP algorithm

Children’s Hospital of Seattle, 2018

- History and physical examination may be suggestive of parapneumonic effusion in children suspected of having CAP, but chest radiography should be used to confirm the presence of pleural fluid. If the chest radiograph is not conclusive, then further imaging with chest ultrasound or computed tomography (CT) is recommended. [LOE: Moderate quality] (Bradley, 2011)

Primary literature evidence (highest level of evidence)*

Source, Year	Summary of findings	Comments	Quality or risk of bias
Latex Agglutination Test (LAT)			
Camargos, 2017	The sensitivity and specificity of LAT was 100% (95% confidence interval, 94.4%–100%) and 83.3% (95% confidence interval, 79.0%–87.0%), respectively, whereas the positive (calculated from Bayes’ theorem) and negative predictive values were, respectively, lower	<ul style="list-style-type: none"> • Diagnostic Test including 418 children and adolescents with mild to moderate CAP acquired pleural effusions hospitalized. 	<ul style="list-style-type: none"> • Low

	<p>than 1% and 100% (95% confidence interval, 98.8%–100%).</p> <p>Positive and negative LR were 6.0 (95% confidence interval, 4.7–7.6) and zero, respectively.</p>	<ul style="list-style-type: none"> • Pleural fluid samples were paired through counterimmunoelectrophoresis (CIE) and latex agglutination test (LAT) 	
Polymerase Chain Reaction			
Munoz-Almagro, 2010	<p>160 patients with pneumococcal pneumonia (145 empyema) had bacterial culture and real-time PCR assays performed.</p> <p>Among them, 41 (24.3%) had positive results for both, 4 (2.4%) had positive culture alone, and 124 (73.3%) had positive real-time PCR alone. The pleural fluid DBL was lower in patients with prior antibiotics ($p = 0.01$) and higher in patients with positive culture ($p < 0.001$). The pleural fluid DBL was positively correlated with serum C-reactive protein ($p=0.009$), pleural fluid neutrophils ($p<0.001$), and pleural fluid glucose ($p<0.001$).</p> <p>The plasma and pleural fluid DBL was higher in patients with ≥ 8 days of hospital stay ($p=0.002$), and the pleural fluid DBL was positively correlated with the number of hours of pleural drainage ($p<0.001$).</p>	<ul style="list-style-type: none"> • Plasma or pleural fluid samples from children and adolescents with confirmed pneumococcal pneumonia were analyzed. • DNA bacterial load (DBL) were correlated with clinical parameters and outcomes. 	<ul style="list-style-type: none"> • Low to moderate

Immunochromatographic Pneumococcal Antigen Test			
Marimon, 2015	<p>Prior to PF extraction, antimicrobial therapy was frequently administered, although blood cultures were obtained before antimicrobial therapy. Only 11 out of 60 CAP patients had received no prior antibiotic dose when PF was analyzed.</p> <p>Of the 60 patients with CAP, a microbial etiology was established in 41 (68.3%); of these, the microorganism was detected in the PF in 40 and in blood culture only in the remaining patient.</p> <p>By culture only, blood and/or PF, a bacterial pathogen was detected in 21.7% of CAP patients, 15.7% by blood culture and 10% by PF culture.</p> <p>In conclusion, despite prior antimicrobial therapy in 49 (81.7%) CAP patients, an etiological diagnosis could be established in 41 (68.3%), 35 being (58.3%) <i>Streptococcus pneumoniae</i>. PF culture was positive in only 6 patients but each molecular test detected more than 82% of cases.</p>	<ul style="list-style-type: none"> • Case-control study – included children and adult patients with and without CAP. • PF specimens were Gram-stained and cultured with and without previous anaerobic broth enrichment onto blood-agar and chocolate-agar plates in a 5% CO₂-enriched atmosphere, and in Brain-Hearth or <i>Schaedler</i> 5% blood-agar plates incubated anaerobically for 24-72 h at 35 degrees Celsius. All PF samples were also tested for the presence of <i>S. pneumoniae</i> by using the immunochromatographic pneumococcal antigen test BINAX-NOW. 	<ul style="list-style-type: none"> • Moderate
Lee, 2012	Of the 62 patient, culture was positive in 3 patients only (4.8%). Pneumococci	<ul style="list-style-type: none"> • 62 exudative parapneumoni 	<ul style="list-style-type: none"> • Low



	<p>were identified in 13 samples (21.0%) by sequencing-confirmed PCR and IT, respectively. When pneumococcal empyema was defined by either positive culture or sequence confirmation, the sensitivity of ICR was 76.9% and the specificity of ICT was 93.9%. Eight of the ten patients with positive ICT and culture-negative results had a history of prior antibiotics use, whereas none of the culture-proved cases had.</p>	<p>c effusions from Korean children were tested with culture, ICT for <i>S. pneumonia</i>, pneumococcal autolysin polymerase chain reaction and subsequent sequencing.</p>	
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Primary literature evidence (lowest level of evidence)*

Source, Year	Summary of findings	Comments	Quality or risk of bias
<p>Polymerase Chain Reaction (PCR) Prasad , 2014</p>	<p>Analysis of aspirated pus demonstrated total leucocyte count >1000 x 10⁶/L, elevated protein (>= 20g/L) and decreased glucose (</- 2.2mmol/L) in 80.3%, 98.5% and 100% respectively. Gram-positive cocci were detected in 29 (43.9) and Gram-negative bacilli in two patients. Nested PCR for the presence of bacterial pathogens were positive in 50% compared with 36.3% for culture</p>	<ul style="list-style-type: none"> • Prospective, hospital-based, cross-sectional study. • After clinical and radiological assessment, diagnostic pleural aspiration was undertaken. • Complete blood count, electrolytes, renal function tests and ELISA for HIV were done. 	<ul style="list-style-type: none"> • Moderate

Quality of evidence (GRADE) - LAT

Risk of bias	Imprecision	Inconsistency	Indirectness	Publication bias	Certainty (Overall)
Low	Imprecise	Consistent	Direct	No	Moderate



Certainty: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Quality of evidence (GRADE) - Polymerase Chain Reaction

Risk of bias	Imprecision	Inconsistency	Indirectness	Publication bias	Certainty (Overall)
Low	Imprecise	Consistent	Direct	No	Moderate

Certainty: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Quality of evidence (GRADE) - Immunochromatographic Pneumococcal Antigen Test

Risk of bias	Imprecision	Inconsistency	Indirectness	Publication bias	Certainty (Overall)
Low	Imprecise	Consistent	Direct	No	Moderate

Certainty: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Question 9. What are the drainage options for parapneumonic effusions?

In 2011, the **Pediatric Infectious Diseases Society and the Infectious Diseases Society of American (IDSA)** recommended the following:

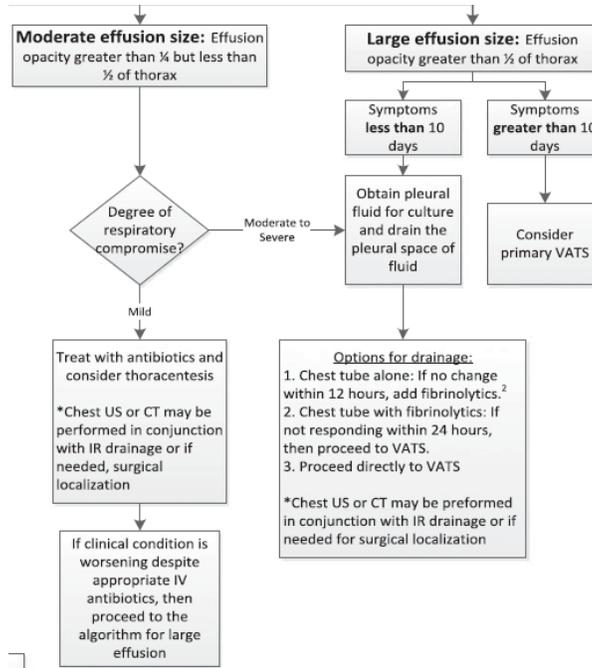
- Small, uncomplicated parapneumonic effusions should not routinely be drained and can be treated with antibiotic therapy alone. **(Strong Recommendation; Moderate Quality Evidence)**
- Moderate parapneumonic effusions associated with respiratory distress, large parapneumonic effusions, or documented purulent effusions should be drained. **(Strong Recommendation; Moderate Quality Evidence)**
- Both chest thoracostomy tube drainage with the addition of fibrinolytic agents and VATS have been demonstrated to be effective methods of treatment. The choice of drainage procedure depends on local expertise. Both of these methods are associated with decreased morbidity compared with chest tube drainage alone. However, in patients with moderate-to-large effusions that are free flowing (no loculations), placement of a chest tube without fibrinolytic agents is a reasonable first option. **(Strong Recommendation; High Quality Evidence)**

The 2018 **Canadian Paediatric Society** stated the following:

- Culture and drainage of a pleural effusion is indicated if the effusion is large and/or is clinically important as a cause for respiratory compromise or when response to medical therapy alone is not satisfactory.

In 2017, the **American Academy of Pediatrics** recommended the following:

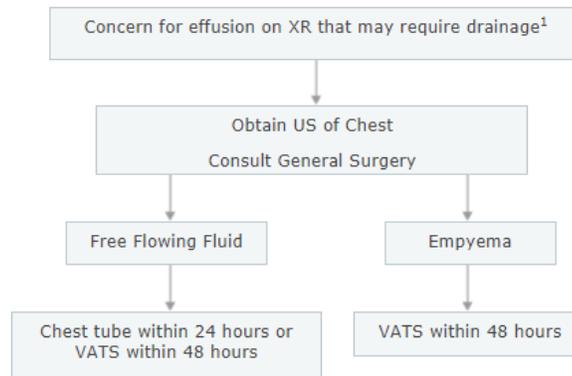
- Large effusion size: Effusion opacity greater than ½ of thorax
 - Symptoms less than 10 days – Obtain pleural fluid for culture and drain the pleural space of fluid
 - Options for drainage:
 - Chest tube alone: If no change within 12 hours, add fibrinolytics
 - Chest tube with fibrinolytics: If not responding within 24 hours, then process to VATS
 - Chest US or CT may be performed in conjunction with IR drainage or if needed, surgical localization



Children’s Hospital of Philadelphia (CHOP), 2017

- Evaluation and Management of Pleural Effusion
 - Concern for effusion on XR that may require drainage
 - Effusions that may require drainage are those that the clinician is concerned are:
 - Large and/or growing in size
 - Impairing pulmonary function
 - Organized and loculated
 - Preventing adequate response to antibiotics
 - Obtain US of Chest; General Surgery
 - Free flowing fluid
 - Chest tube within 24 hours or VATs within 48 hours
 - Empyema
 - VATS within 48 hours

Evaluation and Management of Pleural Effusion



1. Effusions that may require drainage are those that the clinician is concerned are:

1. Large and/or growing in size
2. Impairing pulmonary function
3. Organized and loculated
4. Preventing adequate response to antibiotics

Children’s Hospital of Colorado, 2016 – Followed AAP algorithm

Question 10. When should VATS or open surgical decortication be considered in patients who have had chest tube drainage with or without fibrinolytic therapy?

In 2011, the **Pediatric Infectious Diseases Society and the Infectious Diseases Society of American (IDSA)** recommended the following:

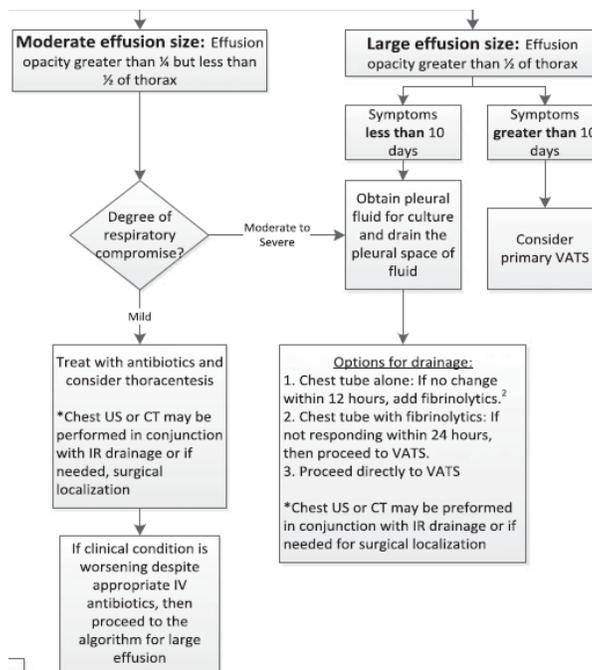
- VATS should be performed when there is persistence of moderate-large effusions and ongoing respiratory compromise despite ~2–3 days of management with a chest tube and completion of fibrinolytic therapy. Open chest debridement with decortication represents another option for management of these children but is associated with higher morbidity rates. **(Strong Recommendation; Low Quality Evidence)**

In 2018, **New South Wales** recommended the following:

- For patients with pleural empyema, Video-assisted thoracoscopic surgery (VATS) or insertion of percutaneous small bore drainage with instillation of fibrinolytics (e.g. 6 doses of urokinase over 3 days) is often required.

In 2017, the **American Academy of Pediatrics** recommended the following:

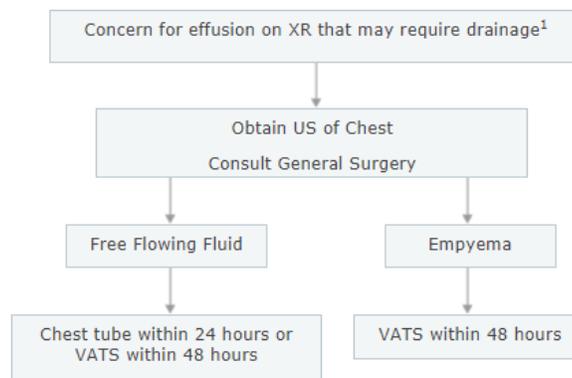
- Large effusion size: Effusion opacity greater than ½ of thorax
 - Symptoms greater than 10 days
 - Consider primary VATS



Children's Hospital of Philadelphia (CHOP), 2017

- Evaluation and Management of Pleural Effusion
 - Concern for effusion on XR that may require drainage
 - Effusions that may require drainage are those that the clinician is concerned are:
 - Large and/or growing in size
 - Impairing pulmonary function
 - Organized and loculated
 - Preventing adequate response to antibiotics
 - Obtain US of Chest; General Surgery
 - Free flowing fluid
 - Chest tube within 24 hours or VATs within 48 hours
 - Empyema
 - VATS within 48 hours

Evaluation and Management of Pleural Effusion



1. Effusions that may require drainage are those that the clinician is concerned are:

1. Large and/or growing in size
2. Impairing pulmonary function
3. Organized and loculated
4. Preventing adequate response to antibiotics

Children's Hospital of Colorado, 2016 – Followed AAP algorithm



Question 11: What is the indication for fibrinolytic therapy for a parapneumonic effusion?

Hospitalized with diagnosis of pneumonia with pleural effusion as documented on chest US and need for intervention in addition to antibiotics based on clinical criteria (respiratory distress, persistent fever)

- No consensus regarding optimal treatment, although chest tubes + fibrinolytics are superior to chest tube alone to facilitate drainage [when tPA warranted]
- No significant difference in clinical outcomes CT+tPA vs. VATS, except cost
 - o Reasonable to use fibrinolytics first line, and move to VATS if resources available upon failure to chemical debridement (~16% expected to fail – consider VATS within 72 hours if loculated empyema drainage rate is suboptimal despite optimal CT-tPA therapy)
 - o “Identifying patients who will not benefit from fibrinolytic treatment is difficult; however, surgical procedures can likely be reserved for patients who fail fibrinolysis.” – Israel et al., 2014

Summary:

- No consensus regarding optimal treatment, although chest tubes + fibrinolytics are superior to chest tube alone to facilitate drainage [when tPA warranted]
- No significant difference in clinical outcomes CT+tPA vs. VATS, except cost
 - o Reasonable to use fibrinolytics first line, and move to VATS if resources available upon failure to chemical debridement (~16% expected to fail – consider VATS within 72 hours if loculated empyema drainage rate is suboptimal despite optimal CT-tPA therapy)



Question 12: What factors determine when it is appropriate to remove a chest tube?

National Guideline Recommendations:

IDSA, 2011

- A chest tube can be removed in the absence of an intrathoracic air leak and when pleural fluid drainage is <1 ml/kg/24 h, usually calculated over the last 12 hours. (strong recommendation; very low-quality evidence)

Evidence Summary:

IDSA, 2011

- Evidence Summary Once a chest tube is placed, either as primary treatment or after VATS, criteria for removal include the absence of an air leak and <1 mL/kg/24 h of pleural fluid drainage, usually calculated over the last 12 hours, or 25–60 mL total in a 24-hour period [92, 266, 267]. This can often be accomplished within 48–72 hours after the operation or completion of fibrinolysis.



Question 13: How parapneumonic effusion should be monitored after chest tube is removed.

No Evidence Found



Question 14: What antibiotic therapy and duration is indicated for the treatment of parapneumonic effusion/empyema?

- Similar to that for CAP without effusion
- Antibiotic therapy should be pathogen directed, based on results of bacterial culture of either blood or pleural fluid
 - If culture-negative or treatment started prior to obtaining fluid, select treatment based on regional epidemiology to provide coverage for the most common pathogens



Question 15: What is the appropriate management of a child who is not responding to treatment for CAP?

If persistent fever, elevated infectious parameters, clinical deterioration after 48-72 hours optimal empiric management:

- Clinical and lab assessment of current severity of illness
- Obtain sputum using flexible bronchoscopy with bronchoalveolar lavage to identify causative pathogens
- Expand coverage using broader spectrum abx (e.g., ceftaroline)

Note: Consensus from experience, versus rigorous studies

Question 16: When can a hospitalized child with CAP be safely discharged?

National Guidelines Recommendations:

IDSA, 2011

- Patients are eligible for discharge when they have documented overall clinical improvement, including level of activity, appetite, and decreased fever for at least 12-24 hours. (Strong recommendation; very low quality evidence)
- Patients are eligible for discharge when they demonstrate consistent pulse oximetry measurements, >90% in room air for at least 12-24 hours (Strong recommendation; moderate quality evidence)
- Patients are eligible for discharge only if they demonstrate stable and/or baseline mental status (strong recommendation; very low quality evidence)
- Patients are not eligible for discharge if they have substantially increased work of breathing or sustained tachypnea or tachycardia (strong recommendation; high quality evidence)
- Patients should have documentation that they can tolerate their home anti-infective regimen, whether oral or intravenous, and home oxygen regimen, if applicable, before hospital discharge (strong recommendation; low quality evidence)
- For infants or young children requiring outpatient oral antibiotic therapy, clinicians should demonstrate that parents are able to administer and children are able to adequately comply with taking those antibiotics before discharge (weak recommendation, very low quality evidence)
- For children who have had a chest tube and meet the requirements listed above, hospital discharge is appropriate after the chest tube has been removed for 12-24 hours, with either no clinical evidence of deterioration since removal, or if a chest radiography was obtained for clinical concerns, radiographic evidence of no significant reaccumulation of parapneumonic effusion or pneumothorax. (strong recommendation; very low quality evidence)
- In infants and children with barriers to care, including concern about careful observation at home, inability to comply with therapy, or inability to be followed-up, these issues should be identified and addressed before discharge (weak recommendation; very low quality evidence)

New South Wales, 2018

- Patients are eligible for discharge when there is overall clinical improvement, good oral intake, resolution of symptoms with consistent pulse oximetry measurements equal to or greater than 95% for at least 12 hours.
- Patients are not appropriate for discharge if they have substantially increased work of breathing or sustained tachypnoea or tachycardia. Parents should be able to administer and children able to comply with taking oral antibiotics prior to discharge.
- If a patient has had a chest tube, the chest tube should have been removed for at least 24 hours prior to discharge

AAP Section on Emergency Medicine

- Discharge Criteria from ER
 - Meets criteria for mild pneumonia
 - Caregiver able to adhere to follow-up
 - Able to tolerate oral medications and hydration

Health System Guidelines:

CHOP, 2019

- Inpatient Discharge Criteria
- Without VATS/chest tube:
Improving within 48-72 hours based upon:
 - Respiratory rate
 - Respiratory effort
 - Fever
 - Oxygen requirement
- After VATS/chest tube:
 - Chest tube out
 - Feeding well
 - No oxygen requirement
 - Fever curve trending down
 - Able to take home antibiotics regimen

Seattle Children's, 2018

Intermountain Healthcare, 2013

- DISCHARGE CRITERIA.
 - Documented overall clinical improvement (decrease fever, increase appetite and activity) for at least 12 hours
 - Consistent pulse oximetry measurements demonstrating adequate oxygenation
 - Normal and/or baseline mental status
 - NO substantially increased work of breathing or sustained tachypnea or tachycardia
 - NO barriers to follow-up or at-home care

CHCO, 2016

- Discharge home
 - Oxygen requirements



Table 4. Maximum oxygen liter flow for discharge

Age of Patient:	Maximum liter flow for discharge:
Less than 24 months and stable	½ liter per minute or less
Older than 24 months and stable	1 liter per minute or less

- Stable and improving hypoxemia and improving clinical status, patients may be discharged home on O2 after 24 hours or more of observation and treatment. These clinical care guidelines are designed to assist clinicians and patients make decisions about appropriate care of the patient with uncomplicated community acquired pneumonia and are not meant as a substitute for sound clinical judgment.
- Reliable follow up and social situation
- Clinical status:
 - Respiratory rate approaching normal as expected for age
 - Normal work of breathing
 - Able to maintain hydration orally
 - Baseline mental status
- Medications
 - Able to take medications orally
 - Able to obtain prescriptions to complete course
- Follow-up
 - Establish PCP follow-up within 2 to 3 days

Children’s Mercy Kansas City

- Overall clinical improvement after a minimum of 12-24 hours
- Consistent pulse oximetry >90% on room air for at least 12-24 hours
- Stable baseline mental status
- Resolved work of breathing/tachypnea
- Documented toleration of oral antibiotics and/or parents have demonstrated ability to administer antibiotics

CHOC Children’s
Discharge Criteria

- Diet tolerated and adequately hydrated
- Vital signs stable
- No supplemental O2 needed for at least 24 hrs
- Meets room air criteria
- Follow-up care coordinated

Question 17: Can pediatric CAP be prevented?

External Guideline Recommendations:

IDSA, 2013

- Children should be immunized with vaccines for bacterial pathogens, including *S. pneumoniae*, *Haemophilus influenzae* type b, and pertussis to prevent CAP. (strong recommendation; high-quality evidence)
- All infants >6 months of age and all children and adolescents should be immunized annually with vaccines for influenza virus to prevent CAP. (strong recommendation; high quality evidence).
- Parents and caretakers of infants <6 months of age, including pregnant adolescents, should be immunized with vaccines for influenza virus and pertussis to protect the infants from exposure. (strong recommendation; weak-quality evidence)
- Pneumococcal CAP after influenza virus infection is decreased by immunization against influenza virus. (strong recommendation; weak-quality evidence)
- High-risk infants should be provided immune prophylaxis with respiratory syncytial virus (RSV)–specific monoclonal antibody to decrease the risk of severe pneumonia and hospitalization caused by RSV. (strong recommendation; high-quality evidence)

AAFP, 2012

- Routine childhood immunization with the pneumococcal conjugate vaccine significantly reduces the incidence of invasive pneumococcal disease in children (Evidence Rating: A)

New South Wales, 2018

- A major factor in the prevention of CAP is the general improvement in public health. Ensuring adequate nutrition, preventing low birth weight and improved hand washing have had good effects in the developed world. However much still needs to be done to improve housing standards, crowding and smoking inside the house especially in the Indigenous community. In addition to this, the uptake of routine vaccinations needs ongoing emphasis by all health professionals

Intermountain Healthcare, 2013

- Screen all patients for influenza, pneumococcal, Hib and/or pertussis immunizations at the clinic or before hospital discharge.
- Promote immunizations for influenza virus and pertussis for all patients and caretakers of infants age <6 months
- Provide influenza antiviral therapy for all children hospitalized with flu

CHCO, 2016

- Prevention



- Hand hygiene
- Isolation procedures
- Influenza and pneumococcal vaccines



Evaluating the Quality of the Evidence

The GRADE criteria were used to evaluate the certainty of evidence reviewed during the development of this guideline. The table below defines how the quality of the evidence is rated and how a strong versus weak recommendation is established. For more detailed information, see Appendix A.

Recommendation	
Strong	Desirable effects clearly outweigh undesirable effects or vice versa
Conditional	Desirable effects closely balanced with undesirable effects
Certainty (Type of Evidence)	
High	Further research is very unlikely to change our confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very Low	Any estimate of effect is very uncertain.

External Guideline Appraisal

A number of associations and health systems have published guidelines regarding CAP in pediatric populations. These guidelines were evaluated according to the University of Pennsylvania’s Center for Evidence-Based Practice Trustworthy Guideline Rating Scale.

External Guidelines for Pediatric CAP

External Guideline	Organization and Author	Last Update	Evidence Evaluation
<i>National Guidelines</i>			
The Management of Community-Acquired Pneumonia in Infants and Children Older Than 3 Months of Age	Pediatric Infectious Diseases Society and the Infectious Diseases Society of America (IDSA)	2011	GRADE
Community-Acquired Pneumonia	American Academy of Family Physicians (AAFP)	2012	Not reported
Community-Acquired Pneumonia in Children	American College of Emergency Physicians	2016	Class of Evidence
Clinical Algorithm for Emergency Department Evaluation and Management of Pediatric Community Acquired Pneumonia	AAP Section on Emergency Medical Committee on Quality Transformation	2017	Not reported
Infants and Children: Acute Management of Community Acquired Pneumonia	New South Wales Government Health	2018	Not reported
Canadian Paediatric Society	Uncomplicated pneumonia in healthy Canadian children youth: Practice points for management	2019	Not reported
<i>Health System Guidelines</i>			
Assessment and Management of Pediatric Community-Acquired Pneumonia (CAP) – patients aged 3 months and older without bronchiolitis	Intermountain Healthcare	2013	Not reported
Uncomplicated Community Acquired Pneumonia	Children’s Hospital Colorado	2016	Not reported
Community Acquired Pneumonia (Without Effusion) Care Guideline	Children’s Hospital of Orange County	2017	Not reported
Pathway for Evaluation and Treatment of Child with Community-Acquired Pneumonia	Children’s Hospital of Philadelphia (CHOP)	2017	Medical evidence and/or clinical consensus
Community-Acquired Pneumonia	Seattle Children’s Hospital	2018	GRADE



External Guideline Ratings

Guideline Issuer, Date	Transparency	Conflict of interest	Development group	Systematic Review	Supporting evidence	Recommendations	External Review	Currency and updates
IDSA, 2011	A	A	B	A	A	A	A	B
AAFP, 2012	C	C	B	B	B	A	C	B
Intermountain, 2013	C	C	C	B	B	B	C	C
ACEP, 2016	A	B	A	A	A	A	A	B
CHCO, 2016	B	C	B	B	B	B	B	A
AAP, 2017	C	C	C	B	B	C	C	B
CHOP, 2017	B	C	B	B		C	C	A
CHOC, 2017	C	C	C	C	B	B	C	B
AAP, 2017	C	C	B	C	C	C	C	B
NSW, 2018	B	C	C	C	C	C	C	A
SCH, 2018	B	C	B	A	A	A	C	A
CPS, 2019	C	C	C	B	B	C	C	A

The guideline rating scale is based on the Institute of Medicine’s “Standards for Developing Trustworthy Clinical Practice Guidelines” (IOM), as well as a review of the AGREE Enterprise and Guidelines International Network domains. See appendix B for full description of the Trustworthy Guideline grading system.

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Appendix A. GRADE criteria for rating a body of evidence on an intervention

Developed by the GRADE Working Group

Grades and interpretations:

High: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low: Any estimate of effect is very uncertain.

Type of evidence and starting level

Randomized trial—high
Observational study—low
Any other evidence—very low

Criteria for increasing or decreasing level

Reductions

Study quality has serious (–1) or very serious (–2) problems
Important inconsistency in evidence (–1)
Directness is somewhat (–1) or seriously (–2) uncertain
Sparse or imprecise data (–1)
Reporting bias highly probable (–1)

Increases

Evidence of association† strong (+1) or very strong (+2)
†Strong association defined as significant relative risk (factor of 2) based on consistent evidence from two or more studies with no plausible confounders
Very strong association defined as significant relative risk (factor of 5) based on direct evidence with no threats to validity.



Appendix B. Trustworthy Guideline rating scale

The University of Pennsylvania’s Center for Evidence-Based Practice Trustworthy Guideline rating scale is based on the Institute of Medicine’s “Standards for Developing Trustworthy Clinical Practice Guidelines” (IOM), as well as a review of the AGREE Enterprise and Guidelines International Network domains.

The purpose of this scale is to focus on the weaknesses of a guideline that may reduce the trust a clinical user can have in the guideline, and distinguish weaknesses in documentation (e.g. guide-line does not have a documented updating process) from weaknesses in the guidance itself (e.g. recommendations are outdated). Current quality scales like AGREE emphasize documentation. They are important checklists for developers of new guidelines, but are less useful for grading existing guidelines. These scales also are harder for clinicians and other persons who are not methodology experts to apply, and their length discourages their use outside formal technology assessment reports. This new scale is brief, balanced, and easy and consistent to apply.

We do not attempt to convert the results of this assessment into a numeric score. Instead we present a table listing the guidelines and how they are rated on each standard. This facilitates qualitative understanding by the reader, who can see for what areas the guideline base as a whole is weak or strong as well as which guidelines are weaker or stronger.

1. Transparency

A	Guideline development methods are fully disclosed.
B	Guideline development methods are partially disclosed.
C	Guideline development methods are not disclosed.

The grader must refer to any cited methods supplements or other supporting material when evaluating the guideline. Methods should include:

Who wrote the initial draft

How the committee voted on or otherwise approved recommendations

Evidence review, external review and methods used for updating are not addressed in this standard.

2. Conflict of interest

A	Funding of the guideline project is disclosed, disclosures are made for each individual panelist, and financial or other conflicts do not apply to key authors of the guideline or to more than 1 in 10 panel members).
B	Guideline states that there were no conflicts (or fewer than 1 in 10 panel members), but does not disclose funding source.
C	Lead author, senior author, or guideline panel members (at least 1 in 10) have conflict of interest, or guideline project was funded by industry sponsor with no assurance of independence.
NR	Guideline does not report on potential conflict of interests.

For purposes of this checklist, conflicts of interest include employment by, consulting for, or holding stock in companies doing business in fields affected by the guideline, as well as related financial conflicts. This definition should not be considered exclusive. As much as anything, this is a surrogate marker for thorough reporting, since it may be assumed that



guideline projects are funded by the sponsoring organization and many authors think it unnecessary to report a non-conflict.

3. Guideline development group

A	Guideline development group includes 1) methodological experts and clinicians and 2) representatives of multiple specialties.
B	Guideline development group includes one of the above, but not both.
C	Guideline developers all from one specialty or organization, and no methodologists.
NR	Affiliations of guideline developers not reported

The purpose of this standard is to ensure that supporters of competing procedures, or clinicians with no vested interest in utilization of one procedure or another, are involved in development of the guideline. Both AGREE II and IOM call for patient or public involvement: very few guideline panels have done so to date, so this is not necessary for guidelines to be rated A. Involvement of methodologists or HTA specialists in the systematic review is sufficient involvement in the guideline development group for our purposes. In the absence of any description of the guideline group, assume the named authors are the guideline group.

4. Systematic review

A	Guideline includes a systematic review of the evidence or links to a current review.
B	Guideline is based on a review which may or may not meet systematic review criteria.
C	Guideline is not based on a review of the evidence.

In order to qualify as a systematic review, the review must do all of the following:

Describe itself as systematic or report search strategies using multiple databases
Define the scope of the review (including key questions and the applicable population)
Either include quantitative or qualitative synthesis of the data or explain why it is not indicated

Note: this element does not address the quality of the systematic review: simply whether or not it exists. Concerns about quality or bias of the review will be discussed in text, where the analyst will explain whether the weaknesses of the review weaken the validity or reliability of the guideline.

Note: a guideline may be rated B on this domain even if the review on which it is based is not available to us. This potential weakness of the guideline should be discussed in text of the report.

5. Grading the supporting evidence

A	Specific supporting evidence (or lack thereof) for each recommendation is cited and graded
B	Specific supporting evidence (or lack thereof) for each recommendation is cited but the recommendation is not graded.
C	Recommendations are not supported by specific evidence.



To score a B on this domain there should be specific citations to evidence tables or individual references for each relevant recommendation in the guideline, or an indication that no evidence was available. Any standardized grading system is acceptable for purposes of this rating. If a guideline reports that there is no evidence available despite a thorough literature search, it may be scored B on this domain, or even A if evidence for other recommendations is cited and graded.

6. Recommendations

A	Considerations for each recommendation are documented (i.e. benefits and harms of a particular action, and/or strength of the evidence); and recommendations are presented in an actionable form.
B	Either one or the other of the above criteria is met.
C	Neither of the above criteria are met

In order to be actionable, the guideline should specify the specific population to which the guideline applies, the specific intervention in question, and the circumstances under which it should be carried out (or not carried out). The language used in the recommendations should also be consistent with the strength of the recommendation (e.g. directive and active language like “should” or “should not” for strong recommendations, and passive language like “consider” for weak recommendations). A figure or algorithm is considered actionable as long as it is complete enough to incorporate all the applicable patients and interventions. Please see the forthcoming NICE manual (24) for a good discussion of actionability in guidelines.

7. External review

A	Guideline was made available to external groups for review.
B	Guideline was reviewed by members of the sponsoring body only.
C	Guideline was not externally reviewed.
NR	No external review process is described.

8. Updating and currency of guideline

A	Guideline is current and an expiration date or update process is specified.
B	Guideline is current but no expiration date or update process is specified.
C	Guideline is outdated.

A guideline is considered current if it is within the developers’ stated validity period, or if no period or expiration data is stated, the guideline was published in the past three years (NOTE: the specific period may be changed at the analyst’s discretion, based on whether the technology is mature and whether there is a significant amount of recent evidence). A guideline must address new evidence when it is updated. A guideline which is simply re-endorsed by the panel without searching for new evidence must be considered outdated



Appendix C. Search Strategy

Question 1:

Search Strategies	Document Strategies Used
<p>Search Terms/Strategies Used:</p>	<p>Database: Ovid MEDLINE(R) <1946 to August Week 4 2019> Search Strategy: -----</p> <ol style="list-style-type: none"> 1 exp Community-Acquired Infections/ (13489) 2 exp Pneumonia/ (88595) 3 1 and 2 (6993) 4 (communit* adj3 acquir* adj7 pneumon*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (9163) 5 3 or 4 (10358) 6 exp Patient Admission/ (23237) 7 5 and 6 (185) 8 ((need* or necessar* or requir* or indicat* or evaluat* or judg* or recommend* or appropriat*) adj3 (((admission* or admit*) adj7 hospital*) or hospitaliz*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (16271) 9 5 and 8 (433) 10 exp Hospitalization/ (224216) 11 5 and 10 (1950) 12 exp Decision Making/ or exp Clinical Decision-Making/ (196920) 13 11 and 12 (38) 14 exp guideline/ or exp guideline adherence/ (61958) 15 11 and 14 (108) 16 exp attitude of health personnel/ or exp professional competence/ or exp physician practice patterns/ (292811) 17 11 and 16 (44) 18 exp Health Status Indicators/ (289724) 19 11 and 18 (479) 20 exp Prognosis/ (1537638) 21 11 and 20 (617) 22 7 or 9 or 13 or 15 or 17 or 19 or 21 (1390) 23 ((need* or necessar* or requir* or indicat* or evaluat* or judg* or recommend* or appropriat*) adj3 (((admission* or admit*) adj7 hospital*) or hospitaliz*) adj10 (communit* adj3 acquir* adj7 pneumon*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (139) 24 22 or 23 (1390) 25 limit 24 to "all child (0 to 18 years)" (353)

Question 2:

Search Strategies	Document Strategies Used
<p>Search Terms/Strategies Used:</p>	<p>Database: Ovid MEDLINE(R) <1946 to August Week 4 2019> Search Strategy: -----</p>



	<p>1 exp Community-Acquired Infections/ (13489) 2 exp Pneumonia/ (88595) 3 1 and 2 (6993) 4 exp Diagnosis/ (8243890) 5 3 and 4 (3026) 6 exp "Sensitivity and Specificity"/ (559473) 7 5 and 6 (407) 8 limit 7 to "all child (0 to 18 years)" (122) 9 ((diagnos* or imag* or test or tests or tested or testing or assay*) adj5 (detect* or recogni* or symptom* or found or find* or identif* or accura* or inaccura* or predict* or efficient* or suitab* or recommend* or prefer* or reliab* or unreliab*) adj10 (communit* adj3 acquir* adj5 pneumon*)).mp. (121) 10 ((diagnos* or imag* or test or tests or tested or testing or assay*) adj5 (detect* or recogni* or symptom* or found or find* or identif* or accura* or inaccura* or predict* or efficient* or suitab* or recommend* or prefer* or reliab* or unreliab*) adj10 CAP).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (498) 11 exp pneumonia/ (88595) 12 10 and 11 (128) 13 9 or 12 (220) 14 limit 13 to "all child (0 to 18 years)" (73) 15 ((diagnos* or imag* or test or tests or tested or testing or assay*) adj5 (detect* or recogni* or symptom* or found or find* or identif* or accura* or inaccura* or predict* or efficient* or suitab* or recommend* or prefer* or reliab* or unreliab*) adj10 (communit* adj3 acquir* adj5 pneumon*) adj15 (child* or infant* or infancy or toddler* or adolescen* or teen*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (17) 16 ((diagnos* or imag* or test or tests or tested or testing or assay*) adj5 (detect* or recogni* or symptom* or found or find* or identif* or accura* or inaccura* or predict* or efficient* or suitab* or recommend* or prefer* or reliab* or unreliab*) adj10 CAP adj15 (child* or infant* or infancy or toddler* or adolescen* or teen*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (25) 17 8 or 14 or 15 or 16 (194)</p>
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Question 3-5:

Search Strategies	Document Strategies Used
Search Terms/Strategies Used:	<p>Database: Ovid MEDLINE(R) <1946 to August Week 4 2019> Search Strategy: ----- 1 exp Community-Acquired Infections/ (13489) 2 exp Pneumonia/ (88595) 3 1 and 2 (6993) 4 exp Anti-Infective Agents/ad, ae, tu, to [Administration & Dosage, Adverse Effects, Therapeutic Use, Toxicity] (687305) 5 exp drug therapy/ (1308791) 6 4 or 5 (1810765) 7 3 and 6 (2841) 8 exp pneumonia/dt (16521) 9 1 and 8 (2879)</p>

- 10 7 or 9 (3261)
- 11 limit 10 to "all child (0 to 18 years)" (729)
- 12 ((drug* or pharma* or antibiot* or anti-biot* or antiinfect* or anti-infect*) adj5 ((communit* adj2 acquir* adj3 infect* adj7 pneumon*) or (communit* adj2 acquir* adj3 pneumon*))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (538)
- 13 limit 12 to "all child (0 to 18 years)" (114)
- 14 11 or 13 (754)
- 15 ((drug* or pharma* or antibiot* or anti-biot* or antiinfect* or anti-infect*) adj5 ((communit* adj2 acquir* adj3 infect* adj7 pneumon*) or (communit* adj2 acquir* adj3 pneumon*)) adj10 (child* or infant or infancy or toddler* or adolesc* or teen*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (39)
- 16 14 or 15 (755)
- 17 remove duplicates from 16 (752)
- 18 limit 17 to (systematic reviews pre 2019 or systematic reviews) (46)
- 19 limit 17 to (adaptive clinical trial or controlled clinical trial or pragmatic clinical trial or randomized controlled trial) (115)
- 20 19 not 18 (114)
- 21 limit 20 to (comparative study or evaluation studies or guideline or validation studies) (64)
- 22 21 not (18 or 19) (0)
- 23 exp "Outcome and Process Assessment (Health Care)"/ (1048425)
- 24 17 and 23 (218)
- 25 exp Epidemiologic Studies/ (2351219)
- 26 17 and 25 (280)
- 27 24 or 26 (398)
- 28 27 not (18 or 19 or 21) (304)
- 29 17 not (18 or 19 or 21 or 27) (288)

Database: Ovid MEDLINE(R) <1946 to August Week 4 2019>

Search Strategy:

-
- 1 exp Community-Acquired Infections/ (13489)
 - 2 exp Pneumonia/ (88595)
 - 3 1 and 2 (6993)
 - 4 exp Anti-Infective Agents/ad, ae, tu, to [Administration & Dosage, Adverse Effects, Therapeutic Use, Toxicity] (687305)
 - 5 exp drug therapy/ (1308791)
 - 6 4 or 5 (1810765)
 - 7 3 and 6 (2841)
 - 8 exp pneumonia/dt (16521)
 - 9 1 and 8 (2879)
 - 10 7 or 9 (3261)
 - 11 limit 10 to "all child (0 to 18 years)" (729)
 - 12 ((drug* or pharma* or antibiot* or anti-biot* or antiinfect* or anti-infect*) adj5 ((communit* adj2 acquir* adj3 infect* adj7 pneumon*) or (communit* adj2 acquir* adj3 pneumon*))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (538)
 - 13 limit 12 to "all child (0 to 18 years)" (114)
 - 14 11 or 13 (754)



	<p>15 ((drug* or pharma* or antibiot* or anti-biot* or antiinfect* or anti-infect*) adj5 ((communit* adj2 acquir* adj3 infect* adj7 pneumon*) or (communit* adj2 acquir* adj3 pneumon*)) adj10 (child* or infant or infancy or toddler* or adolesc* or teen*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (39)</p> <p>16 14 or 15 (755)</p> <p>17 remove duplicates from 16 (752)</p> <p>18 limit 17 to (systematic reviews pre 2019 or systematic reviews) (46)</p> <p>19 limit 17 to (adaptive clinical trial or controlled clinical trial or pragmatic clinical trial or randomized controlled trial) (115)</p> <p>20 19 not 18 (114)</p> <p>21 limit 20 to (comparative study or evaluation studies or guideline or validation studies) (64)</p> <p>22 21 not (18 or 19) (0)</p> <p>23 exp "Outcome and Process Assessment (Health Care)"/ (1048425)</p> <p>24 17 and 23 (218)</p> <p>25 exp Epidemiologic Studies/ (2351219)</p> <p>26 17 and 25 (280)</p> <p>27 24 or 26 (398)</p> <p>28 27 not (18 or 19 or 21) (304)</p> <p>29 17 not (18 or 19 or 21 or 27) (288)</p>
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Question 6:

Search Strategies	Document Strategies Used
<p>Search Terms/Strategies Used:</p>	<p>Database: Ovid MEDLINE(R) ALL <1946 to November 05, 2019> Search Strategy:</p> <p>-----</p> <p>1 exp Pneumonia/ (89284)</p> <p>2 exp Community-Acquired Infections/ (13670)</p> <p>3 1 and 2 (7097)</p> <p>4 (communit* adj3 acquir* adj7 pneumon*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (10666)</p> <p>5 3 or 4 (11872)</p> <p>6 limit 5 to "all child (0 to 18 years)" (2596)</p> <p>7 (communit* adj3 acquir* adj7 pneumon* adj10 (child* or pediatric* or paediatric* or infant* or infancy or toddler* or teen* or adolescen*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (1153)</p> <p>8 6 or 7 (2834)</p> <p>9 (pleura* adj3 effus* adj7 pneumon*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (1894)</p> <p>10 (parapneumo* adj3 effus*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (799)</p>



	<p>11 (parapneumon* adj3 empyem*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (380)</p> <p>12 (pleura* adj3 empyem* adj7 pneumo*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (276)</p> <p>13 (pleura* adj3 empyem*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (4152)</p> <p>14 exp pleural effusion/ (19265)</p> <p>15 9 or 10 or 11 or 12 or 13 or 14 (23569)</p> <p>16 8 and 15 (129)</p> <p>17 ((pleura* or parapneumo*) adj3 (empyem* or effus*) adj7 (diagno* or detect* or identi* or discover* or found or find) adj10 (child* or pediatric* or paediatric* or infant* or infancy or toddler* or teen* or adolescen*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (96)</p> <p>18 16 or 17 (217)</p> <p>19 exp Pleural Effusion/di, dg, mi, pa [Diagnosis, Diagnostic Imaging, Microbiology, Pathology] (8680)</p> <p>20 exp pleural empyema/di, dg, mi, pa (1501)</p> <p>21 19 or 20 (9902)</p> <p>22 8 and 21 (42)</p> <p>23 17 or 22 (135)</p>
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Question 7:

Search Strategies	Document Strategies Used
<p>Search Terms/Strategies Used:</p>	<p>Database: Ovid MEDLINE(R) ALL <1946 to November 05, 2019> Search Strategy:</p> <p>-----</p> <p>1 exp Pneumonia/ (89284)</p> <p>2 exp Community-Acquired Infections/ (13670)</p> <p>3 1 and 2 (7097)</p> <p>4 (communit* adj3 acquir* adj7 pneumon*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (10666)</p> <p>5 3 or 4 (11872)</p> <p>6 limit 5 to "all child (0 to 18 years)" (2596)</p> <p>7 (communit* adj3 acquir* adj7 pneumon* adj10 (child* or pediatric* or paediatric* or infant* or infancy or toddler* or teen* or adolescen*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (1153)</p> <p>8 6 or 7 (2834)</p> <p>9 (pleura* adj3 effus* adj7 pneumon*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading</p>



	<p>word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (1894)</p> <p>10 (parapneumo* adj3 effus*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (799)</p> <p>11 (parapneumon* adj3 empyem*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (380)</p> <p>12 (pleura* adj3 empyem* adj7 pneumo*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (276)</p> <p>13 (pleura* adj3 empyem*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (4152)</p> <p>14 exp pleural effusion/ (19265)</p> <p>15 9 or 10 or 11 or 12 or 13 or 14 (23569)</p> <p>16 8 and 15 (129)</p> <p>17 exp Drainage/ (57715)</p> <p>18 8 and 17 (11)</p> <p>19 ((pleura* or parapneumo*) adj3 (empyem* or effus*) adj7 (drain* or (draw* adj off) or ((remov* or extract* or draw* or withdraw* or tap or siphon* or suction*) adj3 (fluid* or effus* or empyem*))) adj10 (child* or pediatric* or paediatric* or infant* or infancy or toddler* or teen* or adolescen*).mp. (43)</p> <p>20 1 and 14 and 17 (133)</p> <p>21 18 or 19 or 20 (177)</p>
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Question 8:

Search Strategies	Document Strategies Used
<p>Search Terms/Strategies Used:</p>	<p>Database: Ovid MEDLINE(R) ALL <1946 to November 05, 2019></p> <p>Search Strategy:</p> <p>-----</p> <p>1 exp Pneumonia/ (89284)</p> <p>2 exp Community-Acquired Infections/ (13670)</p> <p>3 1 and 2 (7097)</p> <p>4 (communit* adj3 acquir* adj7 pneumon*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (10666)</p> <p>5 3 or 4 (11872)</p> <p>6 limit 5 to "all child (0 to 18 years)" (2596)</p> <p>7 (communit* adj3 acquir* adj7 pneumon* adj10 (child* or pediatric* or paediatric* or infant* or infancy or toddler* or teen* or adolescen*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (1153)</p> <p>8 6 or 7 (2834)</p> <p>9 (pleura* adj3 effus* adj7 pneumon*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading</p>



	<p>word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (1894)</p> <p>10 (parapneumo* adj3 effus*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (799)</p> <p>11 (parapneumon* adj3 empyem*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (380)</p> <p>12 (pleura* adj3 empyem* adj7 pneumo*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (276)</p> <p>13 (pleura* adj3 empyem*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (4152)</p> <p>14 exp pleural effusion/ (19265)</p> <p>15 9 or 10 or 11 or 12 or 13 or 14 (23569)</p> <p>16 8 and 15 (129)</p> <p>17 ((pleura* or parapneumo*) adj3 (empyem* or effus* or fluid* or aspirat*) adj7 (((lab* or microb* or bacteria* or virus* or viral* or diagnos* or clinical*) adj5 (test* or assay* or analy*)) or (analy* adj5 test*))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (427)</p> <p>18 ((pleura* or parapneumo*) adj3 (empyem* or effus* or fluid* or aspirat*) adj10 (((lab* or microb* or bacteria* or virus* or viral* or diagnos* or clinical*) adj7 (test* or assay* or analy*)) or (analy* adj7 test*)) adj15 (child* or pediatric* or paediatric* or infant* or infancy or toddler* or teen* or adolescen*)).mp. (20)</p> <p>19 limit 17 to "all child (0 to 18 years)" (72)</p> <p>20 exp Clinical Laboratory Techniques/ (2541367)</p> <p>21 exp Clinical Laboratory Services/ (848)</p> <p>22 exp Medical Laboratory Science/ (9795)</p> <p>23 20 or 21 or 22 (2550769)</p> <p>24 1 and 14 and 23 (184)</p> <p>25 limit 24 to "all child (0 to 18 years)" (67)</p> <p>26 18 or 19 or 25 (139)</p>
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Question 9:

Search Strategies	Document Strategies Used
<p>Search Terms/Strategies Used:</p>	<p>Database: Ovid MEDLINE(R) ALL <1946 to November 05, 2019></p> <p>Search Strategy:</p> <p>-----</p> <p>1 exp Pneumonia/ (89284)</p> <p>2 exp Community-Acquired Infections/ (13670)</p> <p>3 1 and 2 (7097)</p> <p>4 (communit* adj3 acquir* adj7 pneumon*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (10666)</p> <p>5 3 or 4 (11872)</p> <p>6 limit 5 to "all child (0 to 18 years)" (2596)</p>



	<p>7 (communit* adj3 acquir* adj7 pneumon* adj10 (child* or pediatric* or paediatric* or infant* or infancy or toddler* or teen* or adolescen*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (1153)</p> <p>8 6 or 7 (2834)</p> <p>9 (pleura* adj3 effus* adj7 pneumon*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (1894)</p> <p>10 (parapneumo* adj3 effus*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (799)</p> <p>11 (parapneumon* adj3 empyem*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (380)</p> <p>12 (pleura* adj3 empyem* adj7 pneumo*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (276)</p> <p>13 (pleura* adj3 empyem*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (4152)</p> <p>14 exp pleural effusion/ (19265)</p> <p>15 9 or 10 or 11 or 12 or 13 or 14 (23569)</p> <p>16 8 and 15 (129)</p> <p>17 exp Drainage/ (57715)</p> <p>18 8 and 17 (11)</p> <p>19 ((pleura* or parapneumo*) adj3 (empyem* or effus*) adj7 (drain* or draw* adj off) or ((remov* or extract* or draw* or withdraw* or tap or siphon* or suction*) adj3 (fluid* or effus* or empyem*))) adj10 (child* or pediatric* or paediatric* or infant* or infancy or toddler* or teen* or adolescen*).mp. (43)</p> <p>20 1 and 14 and 17 (133)</p> <p>21 18 or 19 or 20 (177)</p>
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Question 10:

Search Strategies	Document Strategies Used
<p>Search Terms/Strategies Used:</p>	<p>Database: Ovid MEDLINE(R) ALL <1946 to November 05, 2019> Search Strategy:</p> <p>-----</p> <p>1 exp Pneumonia/ (89284) 2 exp Pleural Effusion/ (19265) 3 exp Empyema, Pleural/ (3898) 4 2 or 3 (22608) 5 1 and 4 (1417) 6 ((decorticat* or vats or (video* adj3 assist* adj5 thora* adj5 (surg* or operat* or procedur*))) adj10 (parapneumon* or (pneumon* adj7 (pleura* adj3 (effus* or empyem*))))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (61)</p>



	7 exp Thoracic Surgery, Video-Assisted/ (6598)
	8 5 and 7 (55)
	9 6 or 8 (104)
	10 limit 9 to "all child (0 to 18 years)" (56)
	11 9 not 10 (48)

Question 11:

Search Strategies	Document Strategies Used
Search Terms/Strategies Used:	<p>Database: Ovid MEDLINE(R) ALL <1946 to December 19, 2019> Search Strategy:</p> <p>-----</p> <ol style="list-style-type: none"> 1 exp Fibrinolytic Agents/ad, ae, tu, to [Administration & Dosage, Adverse Effects, Therapeutic Use, Toxicity] (96602) 2 exp Thrombolytic Therapy/ (23751) 3 exp Pneumonia/ (89589) 4 Pleural Effusion/ (16192) 5 exp Empyema/ (8261) 6 4 or 5 (23575) 7 3 and 6 (1892) 8 parapneumon*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (1025) 9 7 or 8 (2589) 10 exp Fibrinolytic Agents/ad, ae, tu, to [Administration & Dosage, Adverse Effects, Therapeutic Use, Toxicity] (96602) 11 exp Thrombolytic Therapy/ (23751) 12 10 or 11 (109027) 13 9 and 12 (161) 14 (fibrinoly* or thromboly* or ((break* or dissolv* or treat* or therap* or interven* or reduc* or remov*) adj3 (clot or clots or clotted*))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (101776) 15 9 and 14 (257) 16 13 or 15 (269)

Question 12-13:

Search Strategies	Document Strategies Used
Search Terms/Strategies Used:	<p>Database: Ovid MEDLINE(R) ALL <1946 to December 19, 2019> Search Strategy:</p> <p>-----</p> <ol style="list-style-type: none"> 1 exp Pneumonia/ (89589) 2 Pleural Effusion/ (16192) 3 exp Empyema/ (8261) 4 2 or 3 (23575) 5 1 and 4 (1892) 6 parapneumon*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (1025) 7 5 or 6 (2589)

- 8 exp Chest Tubes/ (2829)
- 9 exp Thoracostomy/ (1419)
- 10 ((chest* or thora* or pleura*) adj5 (tube* or tubing)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (17161)
- 11 ((chest* or thora* or pleura*) adj5 (drain* or suck* or suction*)).mp. (8789)
- 12 8 or 9 (3734)
- 13 10 or 11 (22353)
- 14 7 and 12 (181)
- 15 7 and 13 (681)
- 16 exp Device Removal/ (12752)
- 17 15 and 16 (1)
- 18 (remov* or ((tak* or pull*) adj2 out*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (637001)
- 19 15 and 18 (42)
- 20 ((stop* or quit* or ceas* or remove) adj5 (treat* or therap* or tube* or intubat*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (24239)
- 21 15 and 20 (1)
- 22 exp Time/ (1335558)
- 23 15 and 22 (29)
- 24 17 or 19 or 21 or 23 (67)
- 25 14 or 24 (226)
- 26 (indicat* adj5 ((chest* or pleura* or thora*) adj3 (tube* or tubing or intub*))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (128)
- 27 12 and 16 (163)
- 28 ((indicat* or sign* or signal* or decis* or decid* or eviden* or hint* or suggest* or recommend*) adj5 (remov* or extract* or ((tak* or pull*) adj2 out)) adj10 ((chest* or pleura* or thora*) adj3 (tube* or tubing or intub*))).mp. (30)
- 29 27 or 28 (184)
- 30 29 not 25 (183)

Database: Ovid MEDLINE(R) ALL <1946 to December 19, 2019>

Search Strategy:

-
- 1 exp Pneumonia/ (89589)
 - 2 Pleural Effusion/ (16192)
 - 3 exp Empyema/ (8261)
 - 4 2 or 3 (23575)
 - 5 1 and 4 (1892)
 - 6 parapneumon*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (1025)
 - 7 5 or 6 (2589)
 - 8 exp Chest Tubes/ (2829)
 - 9 exp Thoracostomy/ (1419)
 - 10 ((chest* or thora* or pleura*) adj5 (tube* or tubing)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading



	<p>word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (17161)</p> <p>11 ((chest* or thora* or pleura*) adj5 (drain* or suck* or suction*)).mp. (8789)</p> <p>12 8 or 9 (3734)</p> <p>13 10 or 11 (22353)</p> <p>14 7 and 12 (181)</p> <p>15 7 and 13 (681)</p> <p>16 exp Device Removal/ (12752)</p> <p>17 15 and 16 (1)</p> <p>18 (remov* or ((tak* or pull*) adj2 out*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (637001)</p> <p>19 15 and 18 (42)</p> <p>20 ((stop* or quit* or ceas* or remove) adj5 (treat* or therap* or tube* or intubat*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (24239)</p> <p>21 15 and 20 (1)</p> <p>22 exp Time/ (1335558)</p> <p>23 15 and 22 (29)</p> <p>24 17 or 19 or 21 or 23 (67)</p> <p>25 14 or 24 (226)</p> <p>26 (indicat* adj5 ((chest* or pleura* or thora*) adj3 (tube* or tubing or intub*))).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (128)</p> <p>27 12 and 16 (163)</p> <p>28 ((indicat* or sign* or signal* or decis* or decid* or eviden* or hint* or suggest* or recommend*) adj5 (remov* or extract* or ((tak* or pull*) adj2 out)) adj10 ((chest* or pleura* or thora*) adj3 (tube* or tubing or intub*))).mp. (30)</p> <p>29 27 or 28 (184)</p> <p>30 29 not 25 (183)</p>
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Question 14:

Search Strategies	Document Strategies Used
<p>Search Terms/Strategies Used:</p>	<p>Database: Ovid MEDLINE(R) ALL <1946 to December 19, 2019></p> <p>Search Strategy:</p> <p>-----</p> <p>1 exp Pneumonia/ (89589)</p> <p>2 Pleural Effusion/ (16192)</p> <p>3 exp Empyema/ (8261)</p> <p>4 2 or 3 (23575)</p> <p>5 1 and 4 (1892)</p> <p>6 parapneumon*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (1025)</p> <p>7 5 or 6 (2589)</p> <p>8 exp Anti-Infective Agents/ (1594320)</p> <p>9 7 and 8 (553)</p> <p>10 exp Drug Therapy/ (1327141)</p> <p>11 dt.fs. (2165459)</p> <p>12 10 or 11 (2886566)</p>



- 13 7 and 12 (589)
- 14 9 or 13 (776)
- 15 limit 14 to (systematic reviews pre 2019 or systematic reviews) (20)
- 16 limit 14 to (controlled clinical trial or randomized controlled trial) (29)
- 17 16 not 15 (29)
- 18 exp "Outcome and Process Assessment (Health Care)"/ (1072769)
- 19 exp Mortality/ (370159)
- 20 mo.fs. (557193)
- 21 18 or 19 or 20 (1685752)
- 22 14 and 21 (199)
- 23 limit 14 to guideline (1)
- 24 22 or 23 (200)
- 25 24 not (15 or 16) (174)
- 26 exp Epidemiologic Studies/ (2409449)
- 27 14 and 26 (177)
- 28 27 not (15 or 16 or 24) (84)
- 29 14 not (15 or 16 or 24 or 28) (469)

Database: Ovid MEDLINE(R) ALL <1946 to December 19, 2019>

Search Strategy:

-
- 1 exp Pneumonia/ (89589)
 - 2 Pleural Effusion/ (16192)
 - 3 exp Empyema/ (8261)
 - 4 2 or 3 (23575)
 - 5 1 and 4 (1892)
 - 6 parapneumon*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (1025)
 - 7 5 or 6 (2589)
 - 8 exp Anti-Infective Agents/ (1594320)
 - 9 7 and 8 (553)
 - 10 exp Drug Therapy/ (1327141)
 - 11 dt.fs. (2165459)
 - 12 10 or 11 (2886566)
 - 13 7 and 12 (589)
 - 14 9 or 13 (776)
 - 15 limit 14 to (systematic reviews pre 2019 or systematic reviews) (20)
 - 16 limit 14 to (controlled clinical trial or randomized controlled trial) (29)
 - 17 16 not 15 (29)
 - 18 exp "Outcome and Process Assessment (Health Care)"/ (1072769)
 - 19 exp Mortality/ (370159)
 - 20 mo.fs. (557193)
 - 21 18 or 19 or 20 (1685752)
 - 22 14 and 21 (199)
 - 23 limit 14 to guideline (1)
 - 24 22 or 23 (200)
 - 25 24 not (15 or 16) (174)
 - 26 exp Epidemiologic Studies/ (2409449)
 - 27 14 and 26 (177)
 - 28 27 not (15 or 16 or 24) (84)
 - 29 14 not (15 or 16 or 24 or 28) (469)

Question 15:



Search Strategies	Document Strategies Used
<p>Search Terms/Strategies Used:</p>	<p>Database: Ovid MEDLINE(R) ALL <1946 to December 19, 2019> Search Strategy:</p> <p>-----</p> <p>1 ("not" adj2 (respond* or effectiv* or success*)) or ("no" adj2 (respons* or effect)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (417123)</p> <p>2 (((("not" adj2 (respond* or effectiv* or success*)) or ("no" adj2 (respons* or effect))) adj7 (treat* or therap* or surg* or interven* or regimen* or pharmacother* or antibiotic* or anti-biotic*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (53039)</p> <p>3 Community-Acquired Infections/ (13741)</p> <p>4 exp Pneumonia/ (89589)</p> <p>5 (community adj3 (acquir* or sourc* or origin* or onset*) adj7 pneumon*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (10786)</p> <p>6 3 and 4 (7153)</p> <p>7 5 or 6 (11984)</p> <p>8 exp Treatment Failure/ (34225)</p> <p>9 (((("not" adj2 (respond* or effectiv* or success*)) or ("no" adj2 (respons* or effect))) adj7 (treat* or therap* or surg* or interven* or regimen* or pharmacother* or antibiotic* or anti-biotic*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (53039)</p> <p>10 ((unsuccess* or fail*) adj7 (treat* or therap* or surg* or interven* or regimen* or pharmacother* or antibiotic* or anti-biotic*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (221031)</p> <p>11 8 or 9 or 10 (270860)</p> <p>12 7 and 11 (588)</p> <p>13 limit 12 to "all child (0 to 18 years)" (127)</p> <p>14 (child* or infant* or infancy or toddler* or teen* or adolesc* or pediatric* or paediatric*).mp. (4003279)</p> <p>15 12 and 14 (151)</p> <p>16 13 or 15 (151)</p>

Question 16:

Search Strategies	Document Strategies Used
<p>Search Terms/Strategies Used:</p>	<p>Database: Ovid MEDLINE(R) ALL <1946 to December 19, 2019> Search Strategy:</p> <p>-----</p> <p>1 (((("not" adj2 (respond* or effectiv* or success*)) or ("no" adj2 (respons* or effect))) adj7 (treat* or therap* or surg* or interven* or regimen* or pharmacother* or antibiotic* or anti-biotic*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (417123)</p>



	<p>2 ((("not" adj2 (respond* or effectiv* or success*)) or ("no" adj2 (respons* or effect))) adj7 (treat* or therap* or surg* or interven* or regimen* or pharmacother* or antibiotic* or anti-biotic*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (53039)</p> <p>3 Community-Acquired Infections/ (13741)</p> <p>4 exp Pneumonia/ (89589)</p> <p>5 (community adj3 (acquir* or sourc* or origin* or onset*) adj7 pneumon*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (10786)</p> <p>6 3 and 4 (7153)</p> <p>7 5 or 6 (11984)</p> <p>8 exp Treatment Failure/ (34225)</p> <p>9 ((("not" adj2 (respond* or effectiv* or success*)) or ("no" adj2 (respons* or effect))) adj7 (treat* or therap* or surg* or interven* or regimen* or pharmacother* or antibiotic* or anti-biotic*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (53039)</p> <p>10 ((unsuccess* or fail*) adj7 (treat* or therap* or surg* or interven* or regimen* or pharmacother* or antibiotic* or anti-biotic*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (221031)</p> <p>11 8 or 9 or 10 (270860)</p> <p>12 7 and 11 (588)</p> <p>13 limit 12 to "all child (0 to 18 years)" (127)</p> <p>14 (child* or infant* or infancy or toddler* or teen* or adolesc* or pediatric* or paediatric*).mp. (4003279)</p> <p>15 12 and 14 (151)</p> <p>16 13 or 15 (151)</p>
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Question 17:

Search Strategies	Document Strategies Used
<p>Search Terms/Strategies Used:</p>	<p>Database: Ovid MEDLINE(R) ALL <1946 to December 19, 2019> Search Strategy:</p> <p>-----</p> <p>1 Community-Acquired Infections/ (13741)</p> <p>2 exp Pneumonia/ (89589)</p> <p>3 (community adj3 (acquir* or sourc* or origin* or onset*) adj7 pneumon*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (10786)</p> <p>4 1 and 2 (7153)</p> <p>5 3 or 4 (11984)</p> <p>6 exp Preventive Health Services/ (580430)</p> <p>7 exp risk/ (1167227)</p> <p>8 6 or 7 (1676382)</p> <p>9 exp Public Health/ (7577536)</p> <p>10 5 and 8 (1960)</p> <p>11 ((prevent* or predict* or immuniz* or vaccin* or control* or deter or deters or deterr* or limit* or hinder* or block* or restrict* or counter* or hinder* or halt* or</p>

imped* or thwart* or avert* or forestall* or restrain* or preclud* or ((reduc* or lower*) adj5 (risk* or chanc* or spread*)) adj7 (pneumon* or cap)).mp. (21988)
 12 9 and 11 (12483)
 13 5 and 12 (1664)
 14 10 or 13 (2994)
 15 limit 14 to "all child (0 to 18 years)" (783)
 16 (child* or infant* or infancy or toddler* or teen* or adolesc* or pediatric* or paediatric*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (4003279)
 17 14 and 16 (853)
 18 15 or 17 (853)
 19 limit 18 to english language (749)
 20 limit 18 to abstracts (822)
 21 19 or 20 (842)
 22 limit 21 to (systematic reviews pre 2019 or systematic reviews) (55)
 23 exp Epidemiologic Studies/ (2409449)
 24 21 and 23 (482)
 25 24 not 22 (474)
 26 21 not (22 or 24) (313)

Database: Ovid MEDLINE(R) ALL <1946 to December 19, 2019>
 Search Strategy:

 1 Community-Acquired Infections/ (13741)
 2 exp Pneumonia/ (89589)
 3 (community adj3 (acquir* or sourc* or origin* or onset*) adj7 pneumon*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (10786)
 4 1 and 2 (7153)
 5 3 or 4 (11984)
 6 exp Preventive Health Services/ (580430)
 7 exp risk/ (1167227)
 8 6 or 7 (1676382)
 9 exp Public Health/ (7577536)
 10 5 and 8 (1960)
 11 ((prevent* or predict* or immuniz* or vaccin* or control* or deter or deters or deterr* or limit* or hinder* or block* or restrict* or counter* or hinder* or halt* or imped* or thwart* or avert* or forestall* or restrain* or preclud* or ((reduc* or lower*) adj5 (risk* or chanc* or spread*)) adj7 (pneumon* or cap)).mp. (21988)
 12 9 and 11 (12483)
 13 5 and 12 (1664)
 14 10 or 13 (2994)
 15 limit 14 to "all child (0 to 18 years)" (783)
 16 (child* or infant* or infancy or toddler* or teen* or adolesc* or pediatric* or paediatric*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] (4003279)
 17 14 and 16 (853)
 18 15 or 17 (853)
 19 limit 18 to english language (749)
 20 limit 18 to abstracts (822)
 21 19 or 20 (842)
 22 limit 21 to (systematic reviews pre 2019 or systematic reviews) (55)



	23	exp Epidemiologic Studies/ (2409449)
	24	21 and 23 (482)
	25	24 not 22 (474)
	26	21 not (22 or 24) (313)