Philippine Practice Guidelines Group in Infectious Diseases (PPGG-ID) - Task Force on Community-Acquired Pneumonia

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Algorithm for the Management-Oriented Risk Stratification of Community-Acquired Pneumonia (CAP) in Immunocompetent Adults

1. Community-Acquired Pneumonia

2. Any of the ff:
   1. RR ≥30/min
   2. PR ≥125/min
   3. Temp ≥40°C or <35°C
   4. Extrapulmonary evidence of sepsis
   5. Suspected aspiration
   6. Unstable co-morbid conditions*
   7. CXR: multilobar, pleural effusion abscess, progression of lesion to >50% of initial within 24 hrs

3. Any of the ff:
   1. Shock or signs of hypoperfusion
      - hypotension
      - altered mental state
      - urine output <30 mL/hr
   2. PaO₂ <60 mmHg or acute hypercapnea (PaCO₂ >50 mmHg)

4. Y
   High risk Community-Acquired Pneumonia

5. N
   Intensive Care

6. N
   Low risk Community-Acquired Pneumonia

7. N
   Moderate risk Community-Acquired Pneumonia

8. Outpatient

9. In-patient

FIGURE 1

Foreword

Since the *Philippine Clinical Practice Guidelines on the Diagnosis, Empiric Management and Prevention of Community-Acquired Pneumonia (CAP)* was published in 1998, new developments in community-acquired pneumonia have emerged. This document aims to provide our physicians with evidence-based approach to the initial antimicrobial management of community-acquired pneumonia in immunocompetent adults.

This 2004 version updates the previous guideline as it incorporates new evidence for its recommendations on the diagnosis, empiric management and prevention of CAP. The major changes that were incorporated in this document include the following:

1. Revision of the risk stratification of community-acquired pneumonia;
2. new criteria for admitting patients with pneumonia case;
3. new recommended initial empiric antibiotic treatment; and
4. updated recommendations on prevention of pneumonia.

It is important to reiterate to our colleagues that by the very nature of this guideline, it cannot encompass all eventualities. Care has been taken to confirm the accuracy of the information presented and to describe generally accepted practices. Therefore, the authors, editors, and publisher of this guideline disclaim any and all liability for errors or omission or for any consequence from the application of information in this document and make no warranty, expressed or implied, with respect to the contents of this publication. Under no circumstance will this guideline suprervene the experience and clinical judgment of the treating physician.

--Task Force on Community-Acquired Pneumonia

Methodology

The evidence-based approach and formal consensus techniques (nominal group technique and the Delphi technique) employed in this year’s update was similar during its initial development. This include the initial phase on preparation of the evidence-based report (EBR) followed by the preparation of the interim report (IR) which is the result of review, discussion of the EBR and consensus of the group. Consensus was defined as 70% of votes cast, either by written ballots or by raising of hands.

The third phase was the preparation of the draft guidelines (DG) which is the result of expert panel review of the IR. This year, the draft of the revised guideline was presented in different convention meetings of different specialties with the intention of soliciting comments, suggestions and opinions from the other specialists and practitioners.

- 2003 Annual Convention of the Philippine Society for Microbiology and Infectious Diseases (PSMID)
- 2004 Annual Convention of the Philippine Academy of Family Physicians (PAFP)
- 2004 Annual Convention of the Philippine College of Chest Physicians (PCCP)
- 2004 Annual Convention of the Philippine College of Physicians (PCP) and the
- 2004 Annual of the Philippine Medical Association (PMA)

The same DG was forwarded to the offices of the following organizations [American College of Chest Physicians - Philippine Chapter (ACCP-PC), Critical Care Nurses Association of the Philippines (CCNAPI), Philippine Academy of Family Physicians (PAFP), Philippine Academy of Medical Specialists (PAMS), Philippine College of Chest Physicians (PCCP), Philippine College of Emergency Medicine and Acute Care (PCEMAC), Philippine College of Physicians (PCP), Philippine College of Radiology (PCR), Philippine Medical Association (PMA), Philippine Nurses’ Association (PNA), Philippine Society for Microbiology and Infectious Diseases (PSMID), Inc., Philippine Tuberculosis Society, Inc. (PTSI)], institutions [Armed Forces of the Philippines Medical Center (AFPMC), Cebu Institute of Medicine (CIM), Davao Doctors’ Hospital (DDH), Department of Health (DOH), Iloilo Doctors’ Hospital (IDH), Lung Center of the Philippines (LCP), Makati Medical Center (MMC), Perpetual Help Medical Center (PHMC), Philippine Heart Center (PHC), Research Institute for Tropical Medicine (RITM), San Lazaro Hospital (SLH), Santo Tomas University Hospital (STUH), St. Luke’s Medical Center (SLMC), University of the East Ramon Magsaysay Memorial Medical Center (UERMMMC), University of the Philippines - Philippine General Hospital (UP-PGH), Veterans Memorial Medical Center (VMMC)], and pharmaceutical companies [Abbott Laboratories, AstraZeneca, Aventis Pasteur, Bayer Philippines, Inc., Bristol-Myers Squibb, Eli Lilly (Phils.), Inc., GlaxoSmithKline, Merck Sharp & Dohme, Pascual Laboratories, Pfizer Philippines, Inc., Roche Philippines, Inc., United Laboratories, Wyeth Philippines, Inc., and Zuellig Pharma.

The final phase is the preparation of the final revised guidelines (FG) which was presented in the midyear convention of PSMID 2004 and again, during the annual convention of PSMID 2004.

The completion of this updated guideline is just the beginning of our continuing commitment to bring this Clinical Practice Guidelines into the utilization phase. After all, “Guidelines do not implement themselves”.

Introduction

Pneumonia is the third leading cause of morbidity (2001) and mortality (1998) in Filipinos based on the Philippine Health Statistics (Department of Health). This clinical practice guideline on community-acquired pneumonia (CA) specific only for the empiric therapy of immunocompetent adults has been drafted to provide the clinician with practical approaches in the resolution of important issues on the diagnosis, management and prevention of CAP in adult patients. This consensus is
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Issues and Recommendations

The following recommendations incorporate updates information related to the seven issues addressed in the 1998 clinical practice guidelines on the diagnosis, treatment and prevention of CAP. The summary of evidence after each recommendation serves as the basis for the consensus statements.

1. Can CAP be diagnosed accurately by history and physical examination?

   - Accuracy of predicting CAP by physicians’ clinical judgment is between 60-76%.
   - Clinical prediction rules combining history and physical examination findings may be utilized to presumptively identify patients with pneumonia.

   Community-acquired pneumonia is a lower respiratory tract infection acquired in the community within 24 hours to less than 2 weeks. It commonly presents with acute cough, abnormal vital signs of tachypnea (RR>20 breaths per minute), tachycardia (CR>100/min), and fever (T>37.8°C) with at least one abnormal chest finding of diminished breath sounds, rhonchi, crackles or wheeze. However, no particular clinical symptom or abnormal finding is sufficiently sensitive or specific to confirm or exclude the diagnosis of community-acquired pneumonia. Clinical prediction rules combining history and physical examination findings may be utilized to presumptively identify patients with pneumonia (Grade B). However, accuracy of predicting CAP by these clinical findings is only between 60-76%. Uncommon presentations of CAP (i.e., minimal physical findings and extrapulmonary symptoms) may partly explain such low accuracy.

   **Summary of Evidence**

   CAP is commonly defined as an acute infection of the pulmonary parenchyma accompanied by symptoms of acute illness accompanied by abnormal chest findings. Patients who acquire the infection in hospitals or long-term facilities are typically excluded from the definition. There is reported significant inter-observer agreement among physicians in obtaining clinical symptoms and signs in diagnosing patients with possible CAP. Patients with atypical pneumonia may present with predominantly extrapulmonary symptoms. Furthermore, elderly patients may not present with classical symptoms of fever, cough and dyspnea.

   **History**

   Prospective cohort trials evaluated the sensitivity and specificity of the clinical history in pneumonia. Using the chest radiograph as the reference for the diagnosis of pneumonia, none of the trials proved that symptoms are important in ruling in or ruling out the diagnosis of pneumonia.

   In a recent review by Metlay et al, symptoms of fever and cough do not distinguish between community-acquired pneumonia from other causes of respiratory illness. As shown in Table 1, the positive likelihood ratio (LR+) for the presence of pneumonia and the negative likelihood ratio (LR-) for the absence of pneumonia are close to 1. This indeterminate ratio of 1 does not generate moderate or large shifts in disease probability.

   **Physical Examination**

   Vital signs of abnormalities on the probability of pneumonia depend on the cut-off value set by studies in defining an abnormal result. A respiratory rate greater than 20 breaths/min resulted in a likelihood ratio of only 1.2 in one study but a respiratory rate greater than 25 breaths/min increased the likelihood ratio to 1.5 to 3.4. In contrast, one study has shown that normal vital signs (RR, HR, and temperature) significantly decreased the probability of community-acquired pneumonia (negative likelihood ratio = 0.18). This result reduced the pretest odds by more than fivefold.

   Like the history in Table 1, abnormal lung findings (e.g. crackles) increase the probability of pneumonia by only a small amount. Egophony (LR+ 2.0 - 8.6) may significantly increase the likelihood of pneumonia. However, its impact may only be modest with positive predictive value ranging from as low as 20% to no higher than 56%. Normal chest examination findings have little effect on the probability of pneumonia with a likelihood ratio of only 0.6.

   **Combination of History and Physical Examination**

   Prediction rules combining history and physical examination significantly affect the probability of pneumonia. Table 2 shows the accuracy of predicting pulmonary infiltrates utilizing the Gennis et al rule and Heckerling et al score. Application of the two studies results in better prediction of community-acquired pneumonia exceeding that of physician’s clinical judgment. These prediction rules may be utilized to help physicians identify patients who may have pneumonia and therefore
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need a chest x-ray.

Three studies have proven that combinations of history and physical examination findings significantly affect the probability of pneumonia. Assuming a baseline prevalence of pneumonia of 5%, a prediction rule may be applied to a patient with acute cough, fever, tachycardia and crakclkes. In this case, the revised probability of pneumonia increases within the range of 18% to 42%. In contrast, the probability of pneumonia is estimated to range from only 1% to 13% in a patient with an acute cough but with normal vital signs.10

Based on cohort studies, there are no clinical features that can reliably distinguish typical from atypical pneumonia.

2. What is the value of the chest radiograph in the diagnosis of CAP?

- For diagnostic certainty in the management of patient with suspected pneumonia, chest radiography should be performed.
- Chest x-ray is also essential in assessing severity of disease and in prognostication.
- It may suggest possible etiology and help differentiate pneumonia from other conditions.

A new parenchymal infiltrate in the chest radiograph remains the reference diagnostic standard for pneumonia (Grade A). Chest radiography should be done to confirm the diagnosis in most patients (Grade A). In patients with moderate to severe illness and with normal initial chest radiograph, a repeat chest radiography after several days should be done to confirm the diagnosis of pneumonia.

In addition to confirming the diagnosis of pneumonia, an initial chest radiographic examination is essential in assessing the severity of disease and presence of complications. Findings of bilateral or multilobar involvement, progression of infiltrates within 24 hours of the initial chest x-ray, pleural effusion, and lung abscess are suggestive of severe disease, poor prognosis and indicate the need for hospital admission. Chest radiography may also suggest possible etiology and help in differentiating pneumonia from other conditions that may mimic it (Grade A).

Summary of Evidence

Physician’s ability to assess community-acquired pneumonia on clinical grounds is low and cannot replace chest radiographs. Consensus statements from professional organizations strongly recommend the need for chest radiography to confirm the diagnosis of community-acquired pneumonia.1, 16 In addition, the chest radiograph is requested to detect associated lung disease, to gain insight into the causative agent (in some cases), to assess severity and as baseline to assess response.1 A different recommendation from a British study suggests that chest radiographs be performed only when there are focal chest signs, when the symptoms worsen with antibiotic therapy or when recovery is slower than expected.16

Although inter-observer variability in the interpretation of x-ray patterns has been cited in the literature, there is general agreement among radiologists as to the presence or absence of infiltrate.17 In a multivariate analysis of patient outcome, radiographic spread or bilateral involvement of pneumonia was related to mortality (See Table 3).18 In a meta-analysis of prognosis and outcome of patients with CAP multi-lobar radiographic pulmonary infiltrates (OR = 3.1; 95% CI, 1.9 - 5.1) was shown to be significantly associated with mortality.19

3. Which patient will need hospital admission?

- A management-oriented risk stratification of CAP based on the patient’s clinical presentation/condition and chest x-ray findings should be utilized in the decision to hospitalize patients with CAP.

The physician’s decision to hospitalize a patient is generally based on the stability of the patient’s clinical condition, the presence or absence of other active medical problems, the risk of death and complications, and sometimes psychosocial considerations. Disease-specific prognostic indicators may be used to assess

<table>
<thead>
<tr>
<th>Type of Finding**</th>
<th>Positive Likelihood Ratioa</th>
<th>Negative Likelihood Ratioa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical History</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fever</td>
<td>1.7 - 2.1</td>
<td>0.6 - 0.7</td>
</tr>
<tr>
<td>Chills</td>
<td>1.3 - 1.7</td>
<td>0.7 - 0.9</td>
</tr>
<tr>
<td>Vital Signs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tachypnea</td>
<td>1.5 - 3.4</td>
<td>0.8</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>1.6 - 2.3</td>
<td>0.5 - 0.7</td>
</tr>
<tr>
<td>Hyperthermia</td>
<td>1.4 - 4.4</td>
<td>0.6 - 0.8</td>
</tr>
<tr>
<td>Chest Examination</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dullness to percussion</td>
<td>2.2 - 4.3</td>
<td>0.8 - 0.9</td>
</tr>
<tr>
<td>Decreased breath sounds</td>
<td>2.3 - 2.5</td>
<td>0.6 - 0.8</td>
</tr>
<tr>
<td>Rhonchi</td>
<td>1.4 - 1.5</td>
<td>0.8 - 0.9</td>
</tr>
<tr>
<td>Egophony</td>
<td>2.0 - 8.6</td>
<td>0.8 - 1.0</td>
</tr>
</tbody>
</table>

* Adapted from Metlay et al10
** Only findings that were statistically significantly associated with the presence and absence of pneumonia in at least two studies were included (P<0.05 in a two-tailed Chi-square or Fisher exact test).

Positive likelihood ratio for pneumonia when finding is present (sensitivity/specifcity) and raises probability of disease (LR >1).

Negative likelihood ratio for pneumonia when finding is absent (1 - sensitivity/specificity) and lowers probability of disease (LR <1).

As explained in this study LR greater than 5 or less than 0.2 generate moderate to large shifts in disease probability.

LR of 2 to 5 and 0.5 to 0.2 generate small changes in disease probability.

LR of 1 to 2 and 0.5 to 1 generate rarely important changes in disease probability.

b Tachypnea defined as respiratory rate >25 breaths/min
c Tachycardia defined as heart rate >100 beats/min in 2 studies and >120 beats/min in a third study.
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the initial severity of pneumonia and guide the physician in the decision to hospitalize a patient. However, these guidelines should always be applied in conjunction with the physician's clinical judgment; the initial decision may be altered depending on the clinical course. Patients with CAP can be classified into three risk categories (See Table 4 to help determine the need for hospitalization. Figure 1 shows the algorithm for management-oriented risk stratification of community-acquired pneumonia in immunocompetent adults.

**Low Risk CAP**

Adult patients with stable vital signs (RR<30 breaths/minute, DBP ≥60 mmHg and SBP ≥90 mmHg, pulse <125 beats/minute, and temperature <40°C) are associated with low morbidity and mortality rate of <5% and are thus categorized as Low Risk CAP. These patients are considered suitable for outpatient care (Grade A).

Those patients with stable comorbid conditions such as controlled diabetes mellitus, neoplastic disease in remission, neurologic disease, congestive heart failure (CHF) class I, coronary artery disease (CAD), immunosuppression (Grade A), renal insufficiency (Grade B), chronic obstructive pulmonary disease (COPD), chronic liver disease, chronic alcohol abuse (Grade C), are also classified under this risk category as they may be treated as out-patients if there is reasonable assurance for follow-up (Grade C).

**Moderate Risk CAP**

Patients with any one of the following physical findings: RR ≥30 breaths/minute, pulse rate ≥125 beats/minute, or temperature <35°C or ≥40°C; those with radiographic findings of bilateral or multilobar involvement, progression of lesion to 50% of initial finding within 24 hours, pleural effusion, abscess; those with suspected aspiration; and those with extrapulmonary evidence of sepsis are associated with a complicated outcome and higher mortality rate of 21% and are thus categorized as Moderate Risk CAP. Patients with unstable comorbid conditions (i.e., uncontrolled diabetes mellitus, active malignancies, progressing neurologic disease, CHF class II-IV, unstable CAD, on high-dose immunosuppressive therapy, renal failure on dialysis, COPD in acute exacerbation, decompensated liver disease, uncontrolled alcohol abuse) which may aggravate or be aggravated by the pneumonia are included in this category. These patients need to be hospitalized for parenteral therapy (Grade A).

**High Risk CAP**

Patients with impending or frank respiratory failure (i.e., hypoxemia with PaO₂<60 mmHg or acute hypercapnea with PaCO₂>50mmHg) or hemodynamic alterations and hypoperfusion (i.e., altered mental state, DBP <60 mmHg or SBP <90 mmHg, or urine output <30 mL/hour) are associated with mortality rate of 36% and are thus categorized as High Risk CAP warranting admission in the intensive care unit (Grade A). Figure 1 is an algorithm which may be used to guide physicians in the decision to hospitalize patients with CAP.

Those patients with history of chronic or prolonged (>7 days within the past month) broad-spectrum antibiotic therapy, bronchiectasis, malnutrition, or steroid therapy are at risk for infection with Pseudomonas aeruginosa and this should be taken into consideration in the choice of antimicrobial therapy.

**Summary of Evidence**

Medical researches have shown that wide variations in clinical practice may occur among physicians, depending on the physician's education and experience. Likewise, analyses of hospital admission rates for CAP show marked variation. This suggests that physicians are using differing criteria for deciding which patients with CAP need to be hospitalized and which patients may be treated as out-patients. In actual practice, physicians most often tend to use their clinical impression of the patient's general clinical appearance when deciding whether or not to hospitalize. It has also been shown that when making a decision about hospitalization for

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**Table 2. Accuracy of predicting pneumonia by physicians' clinical judgment**

<table>
<thead>
<tr>
<th>Decision Basis</th>
<th>Physician's Clinical Judgment</th>
<th>Heckerling et al Score (threshold was 2 points)</th>
<th>Gennis et al Rule (threshold was 1 point)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variables</td>
<td></td>
<td>• Temperature of &gt;37.8°C</td>
<td>• Temperature of &gt;37.8°C</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Pulse of &gt;100/min</td>
<td>• Respiration of &gt;20/min</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Rales</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Decreased breath sounds</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Absence of asthma</td>
<td></td>
</tr>
<tr>
<td>Accuracy in predicting pneumonia</td>
<td>60%</td>
<td>68%</td>
<td>76%</td>
</tr>
</tbody>
</table>

**Table 3. Chest radiographic findings which may predict a complicated course**

<table>
<thead>
<tr>
<th>Chest radiographic findings</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multilobar radiographic pulmonary infiltrate^19</td>
<td>3.1</td>
<td>1.9 - 5.1</td>
</tr>
<tr>
<td>Bilateral pleural effusion^19</td>
<td>2.8</td>
<td>1.4 - 5.8</td>
</tr>
</tbody>
</table>
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any CAP patient, physicians also relied on the patient's respiratory status, the presence of other illnesses and lung involvement of more than one lobe. The evidence for risk stratification comes from several researches which studied the effects of the implementation of a risk-based triage protocol in the admission of patients with community-acquired pneumonia. Analysis of results showed a reduction over all bed-days per patient without any increase in deaths, complications, use of intensive care unit, or re-admissions or any decrement in the health-related quality of life. A prediction rule based on the Pneumonia Severity Index (PSI) validated in more than 50,000 patients from a variety of inpatient and outpatient protocols has emphasized that an age of more than 65 years alone is not an indication for admission. A study by Halm et al has also confirmed that selected low-risk elderly patients with pneumonia can be treated as outpatients with good results. These studies serve as bases for the revised recommendation of not considering age alone as a determinant for admission.

The presence of unstable comorbid conditions as basis for admission is validated by the study of Minohue et al which showed that 7.5% of initially ambulatory patients were subsequently hospitalized within 30 days due to factors related to CAP or due to comorbidity. A meta-analysis on prognosis and outcomes of patients with CAP showed that the presence of diabetes mellitus, neoplastic diseases, or neurologic disease was significantly associated with mortality. Another prospective cohort study also showed the following comorbid illnesses - diabetes mellitus, end-stage renal disease, congestive heart failure -- to be univariate predictors of a complicated course in patients with CAP, while immunosuppression (recent systemic steroid use or cancer chemotherapy), comorbid conditions (diabetes mellitus, congestive heart failure, renal insufficiency), hospitalization within one year of pneumonia presentation, temperature >38.3°C, and high risk etiology (staphylococcal, Gram-negative rod, aspiration or post-obstructive pneumonia) were independent predictors of a complicated course by multivariate analysis. Physical findings of RR ≥ 30 breaths/min, diastolic blood pressure ≥ 60 mmHg or systolic BP < 90 mmHg, pulse ≥ 125/min predict either mortality, increased morbidity, or a complicated course. Laboratory findings of hyperglycemia, azotemia and hypoxemia (defined by an oxygen saturation of less than 90 percent or a partial pressure of arterial oxygen of less than 60 mmHg at room air), and radiographic findings of pleural effusion are independently associated with increased mortality.

4. What microbiologic studies are necessary in CAP?

• In low risk CAP, microbiologic studies are optional.
• In moderate and high risk CAP, blood culture and Gram stain/culture of respiratory specimens should be done.
• When possible, tests to document the presence of Legionella sp. are recommended in hospitalized patients.

In CAP, as with any other infection, the isolation of an etiologic agent is ideal. However, despite adequate studies using good microbiologic techniques, an identifiable pathogen can only be found in 40-60% of cases. In patients with no comorbid disease and low risk for mortality, the most common etiologic agents are still Streptococcus pneumoniae and Haemophilus influenzae. In patients who do not require hospitalization and in whom the etiology is predictable, sputum Gram stain and culture may not be done (Grade B). However for hospitalized patients with moderate to severe CAP, there are more pathogens to consider. In these patients, at least 2 sets of blood cultures are highly recommended. Although of low sensitivity, a positive blood culture is specific and is considered as the gold standard in the etiologic diagnosis of pneumonia. Gram stain and cultures of appropriate pulmonary secretions should also be part of the initial work up (Grade A).

It is difficult to predict the etiology based on symptoms, physical findings and laboratory results. In this document, the term “atypical” is used to refer to a group of organisms (Mycoplasma pneumoniae, Chlamydia pneumoniae, and Legionella pneumophila) rather than to the clinical picture of CAP. Among the atypical pathogens, it is L. pneumophila which causes severe pneumonia with majority of patients requiring intensive care. The associated case fatality rate is high at 5 to 30%. The greatest risk of death occurs in the elderly and immunocompromised patients and delay in treatment is associated with increased mortality. Thus, for all hospitalized patients, it is recommended that we document the presence of atypical pathogens (Grade A).

The most common method for diagnosis of atypical pathogens consists of serology (four-fold rise in IgG titer or high initial titer of IgM), culture and polymerase chain reaction (PCR) of respiratory secretions and tissue. The tests available locally for atypical pathogens include the following: (1) M. pneumoniae: Particle Agglutination Test (serology); (2) C. pneumoniae: Microimmunofluorescence (serology); (3) Legionella sp: urine antigen test and direct fluorescent antibody test of respiratory secretions and tissue.

Invasive procedures such as transtracheal aspirate, lung tap, bronchoalveolar lavage, and protected brush specimens to obtain respiratory secretions for microbiologic studies are reserved for nonresolving pneumonia, immunocompromised patients or when anaerobic pathogens are considered.

The existence of certain epidemiologic (e.g. "SARS", influenza) and clinical conditions like HIV/AIDS which may predispose individuals to infections by co-pathogens including Mycobacterium tuberculosis may dictate the need for further diagnostic investigation.

Summary of Evidence

• Definite etiology: The etiologic diagnosis is consi-dered definite when the pathogen is isolated from uncontami-nated specimens (blood, pleural fluid or secretions obtained from transtracheal or transthoracic aspiration). Pathogens such as M. tuberculosis, Legionella sp., viruses and fungi are not normal colonizers of the upper airway, thus, they are considered definite for the etiology of pneumonia when isolated from respiratory secretions.
• Probable etiology: Pathogens demonstrated by smear or culture isolated in moderate to heavy quantity from
Table 4. Clinical features of patients with CAP according to risk categories

<table>
<thead>
<tr>
<th>Low Risk Cap</th>
<th>Moderate Risk CAP</th>
<th>High Risk CAP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stable vital signs</td>
<td>Unstable vital signs:</td>
<td>Any of the clinical feature of moderate risk CAP plus any of the following:</td>
</tr>
<tr>
<td>• RR &lt;30 breaths/min</td>
<td>• RR ≥30 breaths/min</td>
<td>1. Shock or signs of hypoperfusion</td>
</tr>
<tr>
<td>• PR &lt;125 beats/min</td>
<td>• PR ≥125 beats/min</td>
<td>• hypotension</td>
</tr>
<tr>
<td>• SBP ≥90 mmHg</td>
<td>• Temp ≥40°C or &lt;35°C</td>
<td>• altered mental state</td>
</tr>
<tr>
<td>• DBP ≥60 mmHg</td>
<td></td>
<td>• urine output &lt;30 mL/hr</td>
</tr>
<tr>
<td>No or stable comorbid conditions</td>
<td>Unstable comorbid condition</td>
<td>2. Hypoxia (PaO₂ &lt;60 mmHg) or acute hypercapnea (PaCO₂ &gt;50 mmHg)</td>
</tr>
<tr>
<td>No evidence of extrapulmonary sepsis</td>
<td>(i.e. uncontrolled diabetes mellitus, active malignancies, progressing neurologic disease, congestive heart failure (CHF) Class II-IV, unstable coronary artery disease, renal failure on dialysis, uncompensated COPD, decompensated liver disease)</td>
<td>Chest x-ray:</td>
</tr>
<tr>
<td>No evidence of aspiration</td>
<td>Evidence of extrapulmonary sepsis (hepatic, hematologic, gastrointestinal, endocrine)</td>
<td>• as in moderate risk CAP</td>
</tr>
<tr>
<td>Chest x-ray:</td>
<td>Suspected Aspiration</td>
<td></td>
</tr>
<tr>
<td>• localized infiltrates</td>
<td>Chest x-ray:</td>
<td></td>
</tr>
<tr>
<td>• no evidence of pleural effusion nor abscess</td>
<td>• multilobar infiltrates</td>
<td></td>
</tr>
<tr>
<td>• not progressive within 24 hrs</td>
<td>• pleural effusion or abscess</td>
<td></td>
</tr>
</tbody>
</table>

A sputum Gram stain which shows a predominant morphotype, has an overall sensitivity of 85.1% in predicting the etiology. Gleckman et al showed that patients whose sputum isolated one morphotype in a concentration of <10/10/mL immersion field predicted the blood isolate in 67.7% of the time. This increased to 89.5% in patients with concentration of >10/10/mL immersion field. Another study by Rein revealed a Gram stain sensitivity of 62% and a specificity of 85% in identifying pneumococci in sputum.

Invasive procedures such as transtracheal aspiration, bronchoalveolar lavage, protected specimen brush and lung aspiration are associated with complications and are not routine procedures. These should only be done in patients with nonresolving pneumonia, immunocompromised patients and in those suspected to have anaerobic infection. A specific etiologic agent is isolated in only 40-60% of cultures done. An outpatient study in the Philippines showed that among 197 patients, H. influenzae (19%) and S. pneumoniae (11%) were still predominant etiologic agents. Atypical pathogens (M. pneumoniae, C. pneumoniae and Legionella sp) were seen in 6% of the patients. Local prevalence data in 200339 has identified atypical pathogens as occurring in 43% of samples in hospitalized patients. They occurred either as sole pathogens (11%) or co-pathogens (32%).

Data on the prevalence of atypical organisms in CAP vary widely due to the use of different methods of isolation employed. Each has its own sensitivity and specificity which affect the prevalence of these organisms (see Table 5). Some limitations of these diagnostic tests consist of the following: Cultures of atypical pathogens use media which are not readily available in most clinical laboratories. Culture as well as serology (which compare acute and convalescent sera) tends to be retrospective in nature because of the length of time it takes to get results. Thus, it tends to be useful only in the epidemiologic documentation of the disease. PCR is a promising tool, however, this still needs to undergo standardization.

5. What initial antibiotics are recommended for the empiric treatment of community-acquired pneumonia?
Empiric therapy should be initiated within 4 hours of diagnosis of CAP. Antibiotics, the mainstay for the treatment of pneumonia, should be initiated within 4 hours upon diagnosis of community-acquired pneumonia (Grade B). This recommendation is based on studies which show a reduced in-hospital mortality when antimicrobial therapy is initiated within the first four hours of admission and diagnosis of CAP. Empirical selection of antibiotic therapy should be directed against the likely pathogens (see Table 6). However, this initial empiric therapy should be revised once antimicrobial culture and susceptibility results are available. The dosages of recommended antibiotics in adults weighing 50-60 kg with normal renal and liver function are shown in Table 7.

Low Risk CAP: In previously healthy adult patients judged to have low risk CAP, *S. pneumoniae* and *H. influenzae* are the predominant etiologic agents in more than half of cases where a pathogen is identified. Amoxicillin is considered to be the standard regimen for these patients' outpatient care. In areas with limited resources, cotrimoxazole is a practical cost-effective alternative. Although there is much overlap between individual features of typical and atypical pneumonia, the pattern of extrapulmonary involvement is highly characteristic for atypical organisms such as *Mycoplasma pneumoniae* and *Chlamydophila pneumoniae*, and extended macrolides or azalides may be superior to amoxicillin for patients who have extrapulmonary physical findings.

In patients with stable comorbid illness or those with recent antibiotic therapy, in addition to the above potential pathogens, Gram-negative bacilli may co-exist. Hence, co-amoxiclav, sulbactamin, the second-generation oral cephalosporins (i.e., cefuroxime axetil, or cefacor), or the extended macrolides or azalides are recommended (Grade A). For patients with hypersensitivity to β-lactams, the macrolides may cover for Streptococcus, and fluoroquinolones may also cover Gram-negative bacilli.

Moderate Risk CAP: In patients, with moderate-risk CAP, in addition to *S. pneumoniae* and *H. influenzae*, Gram-negative enteric bacilli are important etiologic considerations; for those with risk of aspiration, infection with anaerobes should also be considered. The empiric regimen of a parenteral non-pseudomonal β-lactam with or without a β-lactamase inhibitor in addition to a macrolide is recommended. Parenteral nonpseudomonal β-lactams include cephalosporins such as cefuroxime sodium, ceftriaxone or cefotaxime. Cefoxitin, cefizoxime or ertapenem are options which also have anaerobic activity (Grade A). Agents which combine a β-lactam with β-lactamase inhibitor include amoxicillin-clavulanic acid or ampicillin-sulbactam. In the higher dose range, these agents also have anaerobic activity.

Combination of any of the regimens with macrolides is now recommended as a significant predominance of *Legionella* was noted among hospitalized patients in a recent local study. An alternative regimen for moderate-risk CAP includes the use of anti-pneumococcal fluoroquinolones alone (Grade A). Although the newer anti-pneumococcal quinolones such as levofloxacin, gatifloxacin or moxfloxacin are also options for therapy, it is recommended that they be reserved as potential second line agents for the treatment of pulmonary tuberculous, particularly for multi-drug resistant tuberculosis (Grade C). For suspected aspiration especially in those with depressed sensorium or seizure episodes, choose a β-lactam with anaerobic activity or add clindamycin or metronidazole to the regimen.

High Risk CAP: Empiric coverage for patients at high risk of mortality from CAP remains essentially the same as that for moderate risk patients. Due to the severity of the condition which may result in a low perfusion state, the parenteral route is recommended for all antimicrobial administration. Modifications to the empiric antibiotic recommendations may be made when the patient is suspected to be at risk of infection by one or more of the following:

**Pseudomonas aeruginosa.** Patients who are at risk of infection with *Pseudomonas aeruginosa* include those with history of chronic or prolonged (>7 days within the past month) use of broad-spectrum antibiotic therapy, with bronchiectasis, malnutrition or use of steroid therapy. For these patients, the recommended empiric therapy should include regimens with (a) a parenteral antipseudomonal β-lactam with or without a β-lactamase inhibitor (b) a parenteral macrolide or anti-pneumococcal fluoroquinolone with or without (c) an aminoglycoside or parenteral ciprofloxacin (Grade A). Anti-pseudomonal β-lactams include ceftazidime, cefepime, or cefpirome. Carbapenems such as meropenem or imipenem-cilastatin have anaerobic activity. Parenteral antipseudomonal β-lactams with β-lactamase inhibitors include piperacillin-tazobactam, ticarcillin-clavulanic acid and sulbactam-cefoperazone.

**Staphylococcus.** In patients shown or suspected to have lung abscesses, pneumatoceles or pyothorax the addition of specific antistaphylococcal agents such as oxacillin should be considered.

**Anaerobes.** In suspected aspiration, clindamycin or metronidazole cover for anaerobes.

**Summary of Evidence**

Initial management decisions on an empiric basis must be made rapidly with a presumptive diagnosis of CAP. Among patients hospitalized for CAP, antibiotic therapy should be initiated within 4 hours after diagnosis has been made. *S. pneumoniae*, *H. influenzae* and atypical pathogens have been demonstrated as the most common causes of low-risk CAP suitable for outpatient care. Table 8 shows the 5 most frequently isolated pathogens in studies done among outpatients and hospitalized patients with CAP. (See Table 8).

The Antimicrobial Resistance Surveillance Program (ARSP) of the Department of Health (DOH) of the Philippines collects antibiotic resistance reports from sentinel hospitals all over the country and publishes a compilation report yearly. Tables 9 and 10 show the resistance rates for *S. pneumoniae* and *H. influenzae* in the last 5 years. In 2003, *S. pneumoniae* resistance rate to penicillin was 9.2%. Thus, unlike other countries, drug resistant *S. pneumoniae* is still not a concern in the Philippines. We can see that the resistance rate to cotrimoxazole is stable at 9.1% and resistance to erythromycin 2.3%. In the same year, *H. influenzae* resistance to ampicillin was 13%. However, the most recent data shows a high
resistance rate of *H. influenzae* to cotrimoxazole (18%). Resistance rate to tetracycline for *S. pneumoniae* and *H. influenzae* has been documented to be high. Thus, for healthy immunocompetent adults without comorbid illness, cotrimoxazole is recommended only as an alternative to amoxicillin and the macrolides. However, in those with comorbidities or those needing hospitalization, with more pathogens to consider, amoxicillin and cotrimoxazole are not viable therapeutic options.

Most of these studies (see Table 8) demonstrate the presence of the atypical pathogens. Macrolides and azalides provide coverage against these potential pathogens. Woodhead40 as well as Mundy et al49 isolated atypical organisms from sputum samples of patients with low risk CAP. Notably, no deaths occurred in this group despite no specific treatment against them. Hence, in the outpatient setting, amoxicillin, which is directed against presumed pneumococcal or *H. influenzae* infection, is considered an adequate regimen.16, 70 Other regimens such as co-amoxiclav, sulfamethoxazole, second-generation oral cephalosporins may be given to patients with CAP who have stable comorbid condition(s) or those with recent antibiotic therapy.71, 72, 73 For CAP patients with extrapulmonary symptoms, an extended macrolide may cover for possible atypical pathogens.74

The group advises the judicious use of fluoroquinolones as an alternative agent in the out-patient setting. A study in the Philippines75 shows that ciprofloxacin and ofloxacin are now significantly less effective alternative therapy in tuberculosis, particularly MDR-TB, a locally hyperendemic disease. This decreased susceptibility of *M. tuberculosis* to quinolones was attributed to a selection pressure from the widespread use of these agents in the community for various infections.76, 77

Studies on etiology among patients with CAP admitted for hospital care showed the predominance of *S. pneumoniae* as well as the occurrence of Gram-negative bacilli. The Asia CAP study among hospitalized CAP patients noted atypical pathogens in 43% of isolates.49 Among the atypical agents, morbidity is significantly increased with Legionella pneumonia; hence, empiric therapy against Legionella is recommended to be part of the regimen for hospitalized patients with CAP along with β-lactam agents which are also effective against Gram-negative bacilli.78, 86 Parenteral erythromycin is the standard regimen for severe Legionella pneumonia. The extended macrolides may be given orally alongside parenteral β-lactam agents among patients with moderate risk CAP if with good gastrointestinal absorption. Newer macrolide agents such as azithromycin, roxithromycin and clarithromycin or the antipneumococcal fluoroquinolones such as levofloxacin, gatifloxacin or moxifloxacin are considered alternatives.86, 94

For patients with risk of infection by *Pseudomonas aeruginosa*, broad spectrum coverage against this high-risk pathogen is recommended.95-103

6. How can response to initial therapy be assessed?

- Response to therapy is expected within 24-72 hours of initiating therapy
- A follow-up chest x-ray is warranted only if with no response to treatment

<table>
<thead>
<tr>
<th>Diagnostic tests for <em>M. pneumoniae</em>40</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory or Tissue Culture</td>
<td>&gt;90</td>
<td>50-90</td>
</tr>
<tr>
<td>Serology (Complement Fixation, ELISA)</td>
<td>75-80</td>
<td>80-90</td>
</tr>
<tr>
<td>PCR</td>
<td>95</td>
<td>95-99</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Diagnostic tests for <em>C. pneumoniae</em>40, 41</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory or Tissue Culture</td>
<td>50-90</td>
<td>?</td>
</tr>
<tr>
<td>Serology</td>
<td>50-90</td>
<td>&gt;85</td>
</tr>
<tr>
<td>(Microimmuno-fluorescence)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCR</td>
<td>&gt;90</td>
<td>&gt;90</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Diagnostic tests for <em>L. pneumophila</em>40, 42</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sputum Culture</td>
<td>75-99</td>
<td>100</td>
</tr>
<tr>
<td>Serology</td>
<td>40-75</td>
<td>95</td>
</tr>
<tr>
<td>Urine Antigen</td>
<td>60-70</td>
<td>99</td>
</tr>
<tr>
<td>PCR</td>
<td>&gt;90</td>
<td>&gt;90</td>
</tr>
<tr>
<td>Direct Fluorescent Antibody Test</td>
<td>25-75</td>
<td>&gt;90</td>
</tr>
</tbody>
</table>

- Streamlining of the empiric antibiotic therapy may be done once the patient shows signs of clinical improvement, has stable vital signs and has a functioning gastrointestinal tract.

Most patients with uncomplicated bacterial pneumonia will respond to treatment within 24-72 hours; re-evaluation of patients, therefore, should be done after 72 hours of initiating therapy. A patient is considered to have responded to treatment if fever declines within 72 hours, temperature normalizes within 5 days and respiratory signs, particularly tachypnea, return to normal. In patients with low risk CAP showing good therapeutic response, a follow-up chest x-ray is not considered necessary. (Grade A)

In hospitalized patients, streamlining initial empiric broad spectrum parenteral therapy to a single narrow spectrum parenteral or oral agent based on available laboratory data, is recommended as early as 72 hours following initiation of empirical treatment. Switch therapy to an oral agent will allow discharge from the hospital as early as the 4th day of hospitalization and will lead to cost-savings (see Table 11). (Grade C)

Table 12 shows the usual recommended dosages of the oral antimicrobial agents for streamlining or switch therapy in adults weighing 50-60 kg with normal renal or liver function.

Based on etiology, the duration of treatment is 5-10 days for bacterial pneumonia, except for enteric-negative pathogens *S. aureus, P. aeruginosa* where treat-
ment should be prolonged to 10-14 days. A two-week period of therapy is recommended for *Mycoplasma* and *Chlamydophilia* pneumoniae while *Legionella* is treated for 14-21 days. A three-day course of oral therapy for low-risk CAP is possible with new agents such as azalides which possess pharmacodynamic characteristics prolonging their duration of effect. (see Table 13).

In patients initially seen after antibiotic therapy has already been initiated, if the choice is among the recommended options and the dosage is correct and the patient has not improved after 72 hours, change the antibiotic. If the dosage is inadequate, correct the dosage and continue the drug.

If there is no response to treatment, patients should be reassessed for possible resistance to antibiotics being given or the presence of other pathogens such as *M. tuberculosis*, viruses, parasites or fungi; treatment should be revised accordingly. Follow-up chest x-ray in these patients may also be helpful in considering other differentials such as pneumothorax, cavitation and extension to previously uninvolved lobes, pulmonary edema and ARDS. In the elderly, *S. pneumoniae* and *L. pneumophila* may be causes of slowly resolving pneumonia. *(Grade A)*

In the absence of any unstable co-existing illness or other life-threatening complication, the patient may be discharged once clinical stability occurs and oral therapy is initiated. (see Table 14)

There is no need to repeat a chest radiograph prior to hospital discharge in a patient who is clinically improving. However, a repeat radiograph is recommended during a follow-up office visit, approximately 4 to 6 weeks after hospital discharge, to establish a new radiographic baseline and to exclude the possibility of malignancy associated with CAP, particularly in older smokers.  

*Summary of Evidence*

Predicted response to any treatment takes into account the immunologic capacity of the host, the severity of the illness, the pathogen and chest radiographic findings. In immunocompetent CAP patients, subjective response is usually noted within 1-3 days of initiation of treatment. Among the clinical parameters of response to therapy, the most carefully documented response is fever or time
### Table 7. Usual recommended dosages of antibiotics in 50-60 KBW adults with normal liver and renal functions

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Dosage</th>
<th>Antibiotic</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low Risk CAP</strong></td>
<td></td>
<td><strong>β-lactams</strong></td>
<td></td>
</tr>
<tr>
<td>(all taken orally)</td>
<td></td>
<td><strong>β-lactams</strong></td>
<td></td>
</tr>
<tr>
<td><strong>ß-lactams:</strong></td>
<td></td>
<td>Co-amoxiclav</td>
<td>625 mg TID or 1 g BID</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>500 mg TID</td>
<td>Sultamicillin</td>
<td>750 mg BID</td>
</tr>
<tr>
<td><strong>Trim/sulfonamide:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cotrimoxazole</td>
<td>160/180 mg BID</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Macrolides:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Azithromycin</td>
<td>500 mg OD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>500 mg BID</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Roxitromycine</td>
<td>150 mg BID or</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>300 mg OD</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Moderate Risk CAP</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Macrolides:</strong></td>
<td></td>
<td><strong>2nd generation cephalosporins:</strong></td>
<td></td>
</tr>
<tr>
<td>Erythromycin IV</td>
<td>0.5 - 1 g q 6 h</td>
<td>Cefuroxime axetil</td>
<td>500 mg BID</td>
</tr>
<tr>
<td>Azithromycin PO or IV</td>
<td>500 mg q 24 h</td>
<td>Cefaclor</td>
<td>500 mg TID or</td>
</tr>
<tr>
<td>Clarithromycin PO or IV</td>
<td>500 mg q 12 h</td>
<td></td>
<td>750 mg BID</td>
</tr>
<tr>
<td>Roxithromycine PO</td>
<td>150 - 300 mg BID</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Antipneumococcal Fluoroquinolones:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Levofoxacin PO or IV</td>
<td>500 mg q 24 h</td>
<td>Cefotaxime IV</td>
<td>1.5 g q 8 h</td>
</tr>
<tr>
<td>Gatifloxacin PO or IV</td>
<td>400 mg q 24 h</td>
<td>Cefotaxime IV</td>
<td>1.5 g q 8 h</td>
</tr>
<tr>
<td>Moxifloxacin PO or IV</td>
<td>400 mg q 24 h</td>
<td>Ceftizoxime IV (with anaerobic activity)</td>
<td>1.2 g q 8 h</td>
</tr>
<tr>
<td><strong>β-lactams w/ β-lactamase inhibitor:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sulbactam-Ampicillin IV</td>
<td>1.5 g q 8 h</td>
<td>Ertapenem IV (with anaerobic activity)</td>
<td>1 g q 24 h</td>
</tr>
<tr>
<td>Co-amoxiclav IV</td>
<td>1.2 g q 8 h</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>High Risk CAP</strong></td>
<td></td>
<td><strong>3rd generation cephalosporins:</strong></td>
<td></td>
</tr>
<tr>
<td>(all routes are intravenous)</td>
<td></td>
<td>Ceftriaxone IV</td>
<td>1.2 g q 24 h</td>
</tr>
<tr>
<td><strong>Macrolides:</strong></td>
<td></td>
<td>Cefotaxime IV</td>
<td>1.2 g q 8 h</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>0.5-1 g q 6 h</td>
<td>Ceftizoxime IV (with anaerobic activity)</td>
<td>1.2 g q 8 h</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>500 mg q 24 h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>500 mg q 12 h</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Fluoroquinolones:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Levofoxacin</td>
<td>500 mg q 24 h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gatifloxacin</td>
<td>400 mg q 24 h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>400 mg q 24 h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>400 mg q 12 h</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Aminoglycosides:</strong></td>
<td></td>
<td>Carabapenem:</td>
<td>1 g q 24 h</td>
</tr>
<tr>
<td>Amikacin</td>
<td>15 mg/kg q 24 h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gentamicin</td>
<td>3 mg/kg q 24 h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Netilmicin</td>
<td>7 mg/kg OD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tobramycin</td>
<td>3 mg/kg q 24 h</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>β-lactams w/ β-lactamase inhibitor:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sulbactam-Ampicillin</td>
<td>1.5 g q 6-8 h</td>
<td>Imipenem</td>
<td>500 mg q 6 h</td>
</tr>
<tr>
<td>Co-amoxiclav</td>
<td>1.2 g q 6-8 h</td>
<td>Meropenem</td>
<td>1.2 g q 8 h</td>
</tr>
<tr>
<td><strong>Others:</strong></td>
<td></td>
<td>Oxacillin</td>
<td>1.2 g q 4-6 h</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>600 mg q 8 h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metronidazole</td>
<td>500 mg q 6-8 h</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Community-Acquired Pneumonia

Table 8. Rank order of etiologic agents of CAP

<table>
<thead>
<tr>
<th>Rank</th>
<th>1st</th>
<th>2nd</th>
<th>3rd</th>
<th>4th</th>
<th>5th</th>
</tr>
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<tbody>
<tr>
<td><strong>OUTPATIENTS</strong></td>
<td></td>
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</tr>
<tr>
<td>Philippines57</td>
<td>H. influenzae</td>
<td>S. pneumoniae</td>
<td>S. pneumoniae</td>
<td>H. influenzae</td>
<td>--</td>
</tr>
<tr>
<td>+ H. influenzae</td>
<td>+ Moraxella sp</td>
<td>+ C. pneumoniae</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sweden48</td>
<td>S. pneumoniae</td>
<td>H. influenzae</td>
<td>M. pneumoniae</td>
<td>Viruses</td>
<td>C. pneumoniae</td>
</tr>
<tr>
<td>Thailand49</td>
<td>C. pneumoniae</td>
<td>M. pneumoniae</td>
<td>S. pneumoniae</td>
<td>mixed</td>
<td>L. pneumophila</td>
</tr>
<tr>
<td>US50</td>
<td>H. influenzae</td>
<td>S. pneumoniae</td>
<td>M. catarrhalis</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Spain51</td>
<td>S. pneumoniae</td>
<td>M. pneumoniae</td>
<td>C. pneumoniae</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Laosanne52</td>
<td>S. pneumoniae</td>
<td>M. pneumoniae</td>
<td>C. pneumoniae</td>
<td>C. burnetii</td>
<td>H. spp.</td>
</tr>
<tr>
<td>Finland53</td>
<td>S. pneumoniae</td>
<td>C. pneumoniae</td>
<td>M. pneumoniae</td>
<td>Viruses</td>
<td>H. influenzae</td>
</tr>
<tr>
<td>Slovenia54</td>
<td>M. pneumoniae</td>
<td>C. pneumoniae</td>
<td>S. pneumoniae</td>
<td>Mixed</td>
<td>--</td>
</tr>
<tr>
<td><strong>IN-PATIENTS</strong></td>
<td></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Philippines55</td>
<td>G(-) bacilli</td>
<td>S. pneumoniae</td>
<td>M. catarrhalis</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Philippines51</td>
<td>S. pneumoniae</td>
<td>M. tuberculosis</td>
<td>Chlamydia spp.</td>
<td>L. pneumophila</td>
<td>M. pneumoniae</td>
</tr>
<tr>
<td>Thailand49</td>
<td>S. pneumoniae</td>
<td>G(-) bacilli</td>
<td>C. pneumoniae</td>
<td>M. pneumoniae</td>
<td>mixed</td>
</tr>
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<td>Spain16</td>
<td>S. pneumoniae</td>
<td>H. influenzae</td>
<td>--</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Japan57, 58</td>
<td>S. pneumoniae</td>
<td>H. influenzae</td>
<td>M. pneumoniae</td>
<td>C. pneumoniae</td>
<td>S. milleri grp.</td>
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<td>Japan59</td>
<td>S. pneumoniae</td>
<td>H. influenzae</td>
<td>M. pneumoniae</td>
<td>C. pneumoniae</td>
<td>S. aureus</td>
</tr>
<tr>
<td>Japan60</td>
<td>S. pneumoniae</td>
<td>H. influenzae</td>
<td>C. pneumoniae</td>
<td>M. pneumoniae</td>
<td>Viruses</td>
</tr>
<tr>
<td>Korea61</td>
<td>S. pneumoniae</td>
<td>K. pneumoniae</td>
<td>C. pneumoniae</td>
<td>P. aeruginosa</td>
<td>S. aureus</td>
</tr>
<tr>
<td>Malaysia62</td>
<td>K. pneumoniae</td>
<td>S. pneumoniae</td>
<td>H. influenzae</td>
<td>M. pneumoniae</td>
<td>P. aeruginosa</td>
</tr>
<tr>
<td>Malaysia63</td>
<td>M. tuberculosis</td>
<td>K. pneumoniae</td>
<td>P. aeruginosa</td>
<td>S. aureus</td>
<td>S. pneumoniae</td>
</tr>
<tr>
<td>US64</td>
<td>S. pneumoniae</td>
<td>G(-) bacilli</td>
<td>Legionella</td>
<td>H. influenzae</td>
<td>--</td>
</tr>
<tr>
<td>Israel65</td>
<td>S. pneumoniae</td>
<td>S. aureus</td>
<td>H. influenzae</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>U. Kingdom96</td>
<td>S. pneumoniae</td>
<td>Viruses</td>
<td>C. pneumoniae</td>
<td>H. influenzae</td>
<td>M. pneumoniae</td>
</tr>
</tbody>
</table>

of defervescence.1,105 Fever associated with severe pneumonia has been observed to decline in 72 hours and to completely disappear in 5 days.104 Leukocytosis usually resolves by day 4.15 Follow-up cultures of blood and sputum are not indicated for patients who respond to therapy.1

Chest radiographic findings usually clear more slowly than clinical findings and multiple radiographs are generally not required.104 Follow-up chest radiography should not be done too early as pneumonic infiltrates may persist unless the patient fails to respond. Follow-up radiography during hospitalization may be indicated to assess the position of a endotracheal tube or central line and to exclude pneumothorax after central line placement or to determine other reasons for failure to respond.1 In addition to progression of disease, possible pulmonary complications such as pleural effusion (10.6%), empyema (5.2%), lung abscess, or atelectasis should be assessed.18,107

With regard to host factors, age and presence or absence of comorbid illness are important determinants of the rate of resolution. The speed of resolution of radiographic infiltrates is inversely related to age and number of lobes involved. Cumulative clearance was noted at 50.6%, 66.7%, 76.7%, 84.5%, 89.7%, 92.6% and 94% in patients examined 2, 4, 6, 8, 12, 20 and 24 weeks, respectively.108 Radiographs of patients less than 50 years old with infiltrates is inversely related to age and number of lobes involved. Cumulative clearance was noted at 50.6%, 66.7%, 76.7%, 84.5%, 89.7%, 92.6% and 94% in patients examined 2, 4, 6, 8, 12, 20 and 24 weeks, respectively.108 Radiographs of patients less than 50 years old with pneumonia due to S. pneumoniae clear by 4 weeks in only 60% of patients.109,110 In older patients, patients with underlying illness (particularly alcoholism or COPD) or patients with extensive pneumonia on presentation, the rate of resolution slows considerably with only 20-30% clearing by 4 weeks.109,110,111 L. pneumophila infection may take substantially longer to clear; only 55% of such infections show complete resolution by 12 weeks.112

Cost considerations favor streamlining of initial parenteral empiric broad-spectrum therapy in patients who show adequate clinical response to a narrow spectrum parenteral agent or an oral agent after 2-3 days. The choice should be based on bacteriologic studies if available.113 Determining when to change from intravenous to oral therapy requires clinical judgment and is likely to depend on the individual patient. In general the following parameters should be taken into account in deciding to change to oral treatment: No clinical indication to continue intravenous antibacterial therapy; decrease in C-reactive protein levels, returning to normal; decrease in leucocyte numbers, returning to normal; normal gastrointestinal absorption; no diarrhea; improved or resolving signs and symptoms of infection; temperature returning to normal; and oral medication is feasible for the patient.114,115,116,117 Table 15 shows the benefits of intravenous to oral sequential antibacterial therapy.114 (see Table 15)

In hospitalized patients with CAP without clinical indications of meningitis or endocarditis, the presence of S. pneumoniae bacteremia at the time of hospital admission is not a contraindication for switching a clinically stable patient from intravenous to oral therapy.118 For pneumonia due to confirmed or suspected enterobacteriaceae, sequential therapy with fluoroquinolones or a 3rd generation oral cephalosporin is appropriate due to their optimal pharmacodynamics; their serum concentration exceeds the MIC50 for many common pathogens responsible for
The improved bioavailability of many new antibiotics allows oral preparations to rapidly achieve adequate serum levels (in patients with a functioning gastrointestinal tract). Compliance is a key issue with oral therapy and thus agents chosen should have minimum side effects, once or twice daily dosing, and be cost-effective.\(^{122}\)

Treatment failure is considered when patients do not respond within 72 hours or in those who deteriorate after an initial response. Important causes of nonresponse related to antimicrobial failure include a pathogen resistant to the antimicrobial treatment or superinfection. In such situations, microbiologic studies including blood cultures should be repeated. Unusual pathogens such as \textit{M. tuberculosis}\(^{27}\) may be the cause of treatment failure. Special stains of lower respiratory secretions for \textit{M. tuberculosis}, atypical mycobacteria, \textit{P. carinii} and endemic fungi and antigen detection for Legionella species should thus be performed. For severe lung infections, microbiologic studies should be done on bronchoalveolar lavage specimens or samples obtained by protected specimen brush.\(^{123}\)

Hemodynamic monitoring and clinical evaluation should be undertaken in high risk CAP to assess for possible severe sepsis with multi-organ failure, DIC and ARDS, hepatic failure, congestive heart failure and gastrointestinal bleeding. Other non-infectious complications including pulmonary embolism, myocardial infarction, lung cancer or other unrecognised immunosuppression may also cause non-response and clinical worsening.

Studies are being designed to examine courses of therapy for 5 to 7 days among outpatients, and for 7 to 10 days for inpatients.\(^{124, 125, 126}\) Drugs that attain high concentrations in pulmonary tissues with prolonged duration of effect such as the azalides may allow a three-day course for low-risk CAP.\(^{127-131}\) The presence of coexisting illness and/or bacteremia, the severity of illness at the onset of antibiotic therapy, and the subsequent hospital course should be considered in determining the duration of antibiotic therapy. Generally, \textit{S. pneumoniae} pneumonia and other bacterial infections should be treated for 5 to 10 days: there are no data showing that a longer duration of therapy is needed for bacteremic patients who have shown good clinical response. Patients with \textit{M. pneumoniae} and \textit{C. pneumoniae} may need longer therapy ranging from 10 to 14 days. Immunocompetent patients with Legionnaire’s disease should receive treatment for 14 to 21 days, whereas patients chronically treated with corticosteroids may require 14 days or longer.\(^{15}\)

### 7. How can CAP be prevented?

- Pneumococcal and influenza vaccines are recommended for the prevention of CAP.

It is apparent that pneumococcal infection is important in community-acquired pneumonia (CAP). During outbreaks of influenza, its impact on CAP is also significant as a result of both primary influenza pneumonia and secondary bacterial pneumonia. Both of these infections may be prevented by the use of currently available pneumococcal and influenza vaccines. Cigarette smoking is a risk factor for pneumonia, and smoking cessation, particularly in patients who have had pneumonia, remains an important preventive strategy for CAP.\(^{15}\)

The Philippine CAP Task Force reviewed the current guidelines for pneumococcal and influenza vaccines of the following groups: (1) Advisory Committee on Immunization Practices (ACIP) of the Centers for Disease Control and Prevention (Atlanta, Georgia); (2) Philippine Foundation for Vaccination (PFV); (3) Philippine Society for Microbiology and Infectious Diseases \textit{generation} (PSMID) Committee on Immunization; (4) Philippine College of Chest Physicians (PCCP) Council on Lung Infections; and (5) Department of Health Technical Working Group for Influenza Prevention and Management.\(^{132, 133, 134, 135, 136}\)

### A. Pneumococcal Vaccine

The pneumococcal vaccine is a 23-valent preparation containing purified capsular polysaccharide of the serotypes responsible for at least 85% to 90% of invasive pneumococcal infections in the US.\(^{132}\) In the Philippines, surveillance data of invasive isolates of \textit{S. pneumoniae} among children with bacteremia/meningitis showed that 92% were vaccine types.\(^{137}\) The pneumococcal vaccine may be useful despite the lack of data on important serotypes among Filipino adults, but the applicability of evidence from foreign literature needs to be studied further.

Pneumococcal vaccine is recommended for the following high risk persons: (a) persons ≥60 years old (\textit{Grade B}); (b) those with certain chronic illnesses such as cardiovascular disease, lung disease, diabetes mellitus (\textit{Grade A}); alcohol abuse, chronic liver disease, CSF leaks (\textit{Grade B}); functional or anatomic asplenia (\textit{Grade A}) ; (c) those with immune system disorders such as naphthric syndrome, HIV infection, hematologic malignancy, generalized malignancies, long-term use of immunosuppressive medications, organ or bone marrow recipients (\textit{Grade C}).

While the ACIP recommends giving the vaccine for persons aged ≥65 years old, in the Philippines the recommended age is ≥60 years because the average life span in the country is lower. There are reports that the ACIP
Community-Acquired Pneumonia

is considering changes to the vaccine recommendations that would include vaccinating all adults aged ≥50 years and listing smokers among those with chronic illnesses who should be vaccinated at an earlier age.40

The pneumococcal vaccine is administered intramuscularly or subcutaneously as one 0.5-mL dose. Routine revaccination of immunocompetent persons previously vaccinated with 23-valent polysaccharide vaccine is not recommended. However, revaccination once is recommended for persons who are at highest risk for serious pneumococcal infection and those who are likely to have a rapid decline in pneumococcal antibody levels, provided that 5 years have elapsed since receipt of the first dose of pneumococcal vaccine. A second dose is recommended for persons with immune system disorders and for persons aged ≥65 years whose first dose was received before the age of 65 years.132 (Grade A)

Pneumococcal vaccine is not recommended for persons with a history of serious allergic reaction to a vaccine component, moderate or severe acute illness, and pregnancy. It is generally considered safe based on clinical experience. Approximately half of persons who received pneumococcal vaccine develop mild, local side effects (e.g. pain at the injection site, erythema, and swelling). Moderate systemic reactions (e.g. fever and myalgias) and severe systemic reactions (e.g. anaphylactic reactions) rarely have been reported. No neurologic disorders (e.g. Guillain-Barre Syndrome) have been associated with administration of pneumococcal vaccine.132

Table 11. Indications for streamlining of antibiotic therapy

| 1. There is less cough and resolution of respiratory distress (normalization of RR) |
| 2. The patient is afebrile for more than 24 hours. |
| 3. The etiology is not a high risk (virulent/resistant) pathogen. |
| 4. There is no unstable comorbid condition or life-threatening complication such as MI, CHF, complete heart block, new atrial fibrillation, supraventricular tachycardia, etc. |
| 5. There is no obvious reason for continued hospitalization such as hypotension, acute mental changes, BUN:Crea of >10:1, hypoxemia, metabolic acidosis, etc. |
| 6. Patient can take or tolerate medicines by the oral route. |

Table 12: Antibiotic dosage of oral agents for streamlining or switch therapy*

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefprozil</td>
<td>500 mg BID</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>500 mg BID</td>
</tr>
<tr>
<td>Cefaclor</td>
<td>500 mg TID or 750 mg BID</td>
</tr>
<tr>
<td>Cefditoren</td>
<td>400 mg OD</td>
</tr>
<tr>
<td>Cefixime</td>
<td>100-200 mg BID</td>
</tr>
<tr>
<td>Cefpodoxime</td>
<td>100-200 mg BID</td>
</tr>
<tr>
<td>Co-amoxiclav</td>
<td>1 g BID</td>
</tr>
<tr>
<td>Sultamicillin</td>
<td>750 mg BID</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>500 mg OD</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>500 mg BID</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>500 mg OD</td>
</tr>
<tr>
<td>Gatifloxacin</td>
<td>400 mg OD</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>400 mg OD</td>
</tr>
</tbody>
</table>

* in adults, 50-60 KBW with normal liver and renal function

B. Influenza Vaccine

Influenza vaccine is recommended for any person who are at increased risk for complications from influenza (see Table 17). High risk persons for whom influenza vaccination include the following: (a) persons aged ≥50 years, (b) those with chronic illnesses (e.g., lung diseases, cardiovascular diseases, diabetes mellitus, renal dysfunction, hemoglobinopathies); (c) immune system disorders (e.g., HIV infection, malignancies, use of immunosuppressive drugs, radiation therapy, organ or bone marrow transplantation); (d) residents of nursing homes and other chronic care facilities. (Grade A) In addition, health care workers and other persons (including household members) in close contact with persons at high risk should be vaccinated to decrease the risk for transmitting influenza to persons at high risk.133 (Grade A)

The vaccine can also be effective in preventing secondary complications and reducing the risk for influenza-related hospitalizations and death among adults >65 years with or without high-risk medical conditions.138,139 Persons 50 to 64 years of age who do not have high-risk conditions also benefit from vaccination through decreased rates of influenza, decreased absenteeism from work, and decreased need from medical visits and medication, including antibiotics.

In September 2003, amid concerns for recurrence of the SARS outbreak, the WHO called for vaccination of people at high risk of contracting influenza as a matter of urgency. Those in high risk groups include the elderly, people with weakened immune systems, people with underlying chronic diseases, and health care workers who have frequent contact with these vulnerable populations. These WHO recommendations are especially
The influenza vaccine is modified each year to contain antigens of the influenza strains that are anticipated to cause problems in the coming season. Updates in influenza vaccine composition should ensure the closest possible match between the influenza vaccine strains and the circulating influenza strains; ensuring this match is one of the foundations for influenza vaccine efficacy. Information on circulating strains and epidemiological trends is gathered by the WHO Global Influenza Surveillance Network. The Network currently consists of 112 national influenza centres in 83 countries and 4 WHO Collaborating Centres for Reference and Research on Influenza located in Atlanta, United States; London, United Kingdom; Melbourne, Australia; and Tokyo, Japan. Based on information collected by the Network, WHO makes recommendations twice a year on the composition of the influenza vaccine that targets the 3 most virulent strains in circulation.

In the Philippines, influenza is characterized by several epidemics each year, with two main peaks. A large peak occurs during the rainy season from June to September, particularly from July to August. A peak is noted during the months of December to January. Based on a more recent 5-year epidemiologic data (February 1998-September 2003) from the Influenza Virus Surveillance of the Research Institute of Tropical Medicine (RITM), increased influenza activity can be seen from July to October. It is therefore recommended that vaccination should be given once a year 2-3 months before the start of the influenza season.

In adults, the influenza vaccine is administered at a dose of 0.5 mL intramuscularly every year. Annual vaccination with the current vaccine is necessary because immunity declines during the year after vaccination. Inactivated influenza vaccine should not be administered to persons known to have anaphylactic hypersensitivity to eggs or to other components of the influenza vaccine. However, persons who have a history of anaphylactic hypersensitivity to vaccine components but who are also at high risk for complications from influenza can benefit from vaccine after appropriate allergy evaluation and desensitization.

The most frequent side effect of vaccination is soreness at the vaccination site (affecting 10-64%) that lasts less than 2 days. Among older persons and healthy young adults, administration of influenza vaccine is not associated with higher rates of systemic symptoms (e.g. fever, malaise, myalgia and headache) when compared to placebo.

The 1976 swine influenza vaccine was associated with increased frequency of Guillain-Barre Syndrome (GBS). Evidence for a causal relation of GBS with subsequent vaccines prepared from other influenza viruses is unclear. The likelihood of coincidentally experiencing GBS after influenza vaccination is expected to be greater among persons with a history of GBS than among persons with no history of this syndrome. Whether influenza vaccination specifically might increase the risk for recurrence of GBS is unknown; therefore, avoiding vaccinating persons who are not at high risk for severe influenza complications and who are known to have experienced GBS within 6 weeks after a previous influenza vaccination is prudent.

Both pneumococcal and influenza vaccines can be administered simultaneously at different sites without increasing side effects. There is no contraindication for use of either pneumococcal or influenza vaccine immediately after an episode of pneumonia.

There is no evidence from published literature that the use of lyophilized bacterial lysate is effective in preventing pneumonia.

Summary of Evidence

The pneumococcal vaccine is both cost effective and protective against invasive pneumococcal infection when administered to immunocompetent persons. Therefore, all persons in these categories should receive the 23-valent pneumococcal vaccine. Post-licensure epidemiologic studies have documented the vaccine’s efficacy in preventing invasive pneumococcal disease among the elderly and individuals with certain chronic medical conditions. Only one case-control study failed to demonstrate effectiveness against bacteremic disease, possibly because of study limitations such as small sample size and incomplete ascertainment.
of patients’ vaccination status. Moreover, the severity of underlying clinical conditions of case patients may not have been comparable to that of the controls, creating a potentially biased underestimate of vaccine effectiveness. The overall efficacy against invasive pneumococcal disease among immunocompetent persons 65 years of age and older is 75%; however, efficacy seems to decrease with advancing age.146

One recent study by Jackson et al.,147 conducted in a large population of older adults, support the effectiveness of the pneumococcal polysaccharide vaccine for the prevention of bacteremia 0.56 (0.33-0.93). There was no significant association between vaccination and the risk of outpatient pneumonia and death, but vaccination was associated with a significantly higher risk of hospitalization with community-acquired pneumonia, which underscores the critical need to evaluate other vaccine formulations for the prevention of noninvasive pneumococcal infections in adults.

The effectiveness of influenza vaccine depends primarily on the age and immunocompetence of the vaccine recipient and the degree of similarity between the viruses in the vaccine and those in circulation.133 The vaccine prevents influenza illness in approximately 70-90% of healthy adults aged <65 years.148, 149 Influenza vaccination reduces the rates of visits to physicians, sick leave, and antibiotic use attributable to influenza-like illness by 34 to 44%, 32 to 45%, and 25%, respectively.150

Older persons with certain chronic diseases might develop lower postvaccination antibody titers than healthy young adults and thus remain susceptible to influenza-related upper respiratory infection. A randomized trial among non-institutionalized persons >60 years reported a vaccine efficacy of 58% against respiratory illness, but indicated that efficacy might be lower among those aged >70 years.142

A meta-analysis of 20 cohort studies showed that influenza vaccine reduces the risk for pneumonia, hospitalization and death among elderly persons during an influenza epidemic if the vaccine strain is identical or similar to the epidemic strain. Pooled estimates of vaccine efficacy were 53% (95% CI = 35% - 66%) for preventing pneumonia, 56% (95%, CI = 39% - 68%) for preventing respiratory illness, 50% (95% CI = 28% - 65%) for preventing hospitalization, and 68% (95% CI = 56% - 76%) for preventing death. Vaccine efficacy from case-control studies ranged from 32% - 45% for preventing hospitalization due to pneumonia, 31% - 65% for preventing hospital deaths from pneumonia and influenza, 43% - 50% for preventing hospital deaths from all respiratory causes, and 27% - 30% for preventing death from all causes.138

References
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Table 16. Recommendations for pneumococcal vaccination

<table>
<thead>
<tr>
<th>Indications</th>
<th>Adult Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persons aged ≥60 yrs</td>
<td>0.5 mL IM or SC (one-time revaccination may be given after 5 years)</td>
</tr>
<tr>
<td>Chronic Illness: Chronic pulmonary diseases (COPD, bronchiectasis, chronic PTB), cardiovascular, diabetes mellitus, chronic liver disease, chronic renal failure or nephrotic syndrome, functional or anatomic asplenia</td>
<td></td>
</tr>
<tr>
<td>Immunosuppression: HIV, congenital immunodeficiency, malignancies, organ or bone marrow transplantation, chemotherapy, long-term systemic corticosteroids</td>
<td></td>
</tr>
<tr>
<td>Residents of nursing homes &amp; other long-term care facilities</td>
<td></td>
</tr>
<tr>
<td>Pregnant women on their 2nd or 3rd trimester who have not received the flu vaccine w/in the last 12 months</td>
<td></td>
</tr>
<tr>
<td>Any person who desires to reduce the likelihood of acquiring infections</td>
<td></td>
</tr>
</tbody>
</table>

Table 17. Recommendations for influenza vaccination

<table>
<thead>
<tr>
<th>Indications</th>
<th>Adult Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persons aged ≥50 yrs</td>
<td>0.5 mL IM once a year</td>
</tr>
<tr>
<td>Chronic Illness: Chronic pulmonary disease (COPD, asthma, bronchiectasis, chronic PTB), chronic cardiovascular disease, metabolic diseases (diabetes mellitus), renal dysfunction, hemoglobinopathies</td>
<td></td>
</tr>
<tr>
<td>Immunosuppression: HIV, malignancies, immunosuppressive drugs, radiation therapy, organ or bone marrow transplantation</td>
<td></td>
</tr>
<tr>
<td>Residents of nursing homes &amp; other chronic care facilities</td>
<td></td>
</tr>
<tr>
<td>Pregnant women on their 2nd or 3rd trimester who have not received the flu vaccine w/in the last 12 months</td>
<td></td>
</tr>
<tr>
<td>Health care workers &amp; other personnel of outpatient care settings, hospitals, nursing homes, and chronic care facilities</td>
<td></td>
</tr>
<tr>
<td>Persons who provide essential &amp; emergency community services (policemen, firemen, disaster &amp; relief workers)</td>
<td></td>
</tr>
<tr>
<td>Students &amp; other persons in institutional settings (military, prisons, dormitories)</td>
<td></td>
</tr>
<tr>
<td>Any person who desires to reduce the likelihood of becoming ill with influenza</td>
<td></td>
</tr>
</tbody>
</table>

Precautions/Contraindications
- Serious allergic reaction to a vaccine component
- Moderate or serious acute illness
- Pregnancy


Appendix I
Grading System for Recommendations

Categories reflecting the strength of recommendations:

GRADE DEFINITION
A Good evidence to support a recommendation for use
B Moderate evidence to support a recommendation for use
C Poor evidence to support a recommendation for or against use
D Moderate evidence to support a recommendation against use
E Good evidence to support a recommendation against use

Appendix II
Quality filters in assessing the evidence from the literature

1. Studies on effectiveness of treatment and accuracy of diagnostic tests

Criteria for evaluating quality of evidence

a. A randomized controlled trial (RCT) that demonstrates a statistically significant difference in at least one major outcome variable: survival or death OR if the difference is not statistically significant, an RCT of adequate sample size to exclude 25% difference in relative risk with 80% power, given the observed results.

b. An RCT that does not meet the level 1 criteria

c. A non-randomized trial with concurrent controls selected by some systematic method (not selected on the basis of perceived suitability for one treatment of the treatment options)

D. Before-after study or case series of at least 10 patients with historical controls or controls drawn from other studies.

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50

e. Case series of at least 10 patients without controls
f. Case series fewer than 10 patients or case reports

Level of Quality of Evidence for Treatment Trials:

<table>
<thead>
<tr>
<th>Level</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>I.</td>
<td>Evidence from at least one properly randomized controlled trial (Criteria a and b are satisfied)</td>
</tr>
<tr>
<td>II.</td>
<td>Evidence from at least one well-designed clinical trial without randomization, from cohort or case-control analytic studies (preferable from more than one center), from multi-time series, or from dramatic results in uncontrolled experiments (criteria 3-6 above)</td>
</tr>
<tr>
<td>III.</td>
<td>Evidence from opinions of respected authorities on the basis of clinical experience, descriptive studies, or report of expert committees.</td>
</tr>
</tbody>
</table>

2. Studies on the Accuracy of Diagnostic Tests

Criteria for evaluating quality of evidence of studies on the accuracy of diagnostic tests:

a. There was an independent interpretation of the result of the diagnostic test (without knowledge of the result of the gold standard).
b. There was an independent interpretation of the result of the gold standard (without the knowledge of the result of the diagnostic test).
c. The study patients consisted of >50 consecutive patients suspected (but not known) to have the disorder of interest.
d. The diagnostic test and the gold standard are both described in sufficient detail to allow reproducibility.
e. The study population consists of at least 50 patients with and 50 patients without the disorder of interest.

Level of quality of evidence based on a study of the accuracy of a diagnostic test:

<table>
<thead>
<tr>
<th></th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>a + b + c + d</td>
</tr>
<tr>
<td>II</td>
<td>a + b + e + d</td>
</tr>
<tr>
<td>III</td>
<td>Retrospective study</td>
</tr>
<tr>
<td>IV</td>
<td>Patients were non-consecutive, selected because of definitive results of the finding under study.</td>
</tr>
<tr>
<td>V</td>
<td>Unclear gold standard or poorly defined population.</td>
</tr>
</tbody>
</table>

3. Studies on prognosis or causation

Criteria for assessing quality of evidence

A. An inception cohort was chosen
B. Reproducible inclusion and exclusion criteria were used
C. Follow-up was complete for at least 80% of subjects
D. Statistical adjustment was carried out for confounders or extraneous factors
E. Reproducible descriptions of outcome measures were used

Level of Quality of Evidence

<table>
<thead>
<tr>
<th></th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>All of the following criteria must be satisfied</td>
</tr>
<tr>
<td>II</td>
<td>An inception cohort was selected but only 3 or 4 remaining criteria were satisfied.</td>
</tr>
<tr>
<td>III</td>
<td>An inception cohort was selected but only 2 or 4 remaining criteria were satisfied.</td>
</tr>
<tr>
<td>IV</td>
<td>An inception cohort was selected but only 1 or 4 remaining criteria were satisfied.</td>
</tr>
<tr>
<td>V</td>
<td>An inception cohort was selected but only 1 or 4 remaining criteria were satisfied.</td>
</tr>
<tr>
<td></td>
<td>None of the criteria was met.</td>
</tr>
</tbody>
</table>

4. Review Articles

Criteria for evaluating quality of evidence

A. Comprehensive search for evidence.
B. Avoidance of bias in the selection of articles.
C. Assessment of the validity of each cited article.
D. Conclusions supported by the data and analysis presented.

Level of quality of evidence based on above criteria

<table>
<thead>
<tr>
<th></th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>All of the following criteria must be met.</td>
</tr>
<tr>
<td>II</td>
<td>3 of the 4 criteria are met.</td>
</tr>
<tr>
<td>III</td>
<td>1 of the 4 criteria is met.</td>
</tr>
<tr>
<td>IV</td>
<td>1 of the 4 criteria is met.</td>
</tr>
<tr>
<td>V</td>
<td>None of the 4 criteria are met.</td>
</tr>
</tbody>
</table>
### Aminoglycosides

**Amikacin**  
Amikacide  
Amikin  
Cidacid  
Kormakin

**Gentamicin**  
Servigenta

**Netilmicin**  
Netromycin

### Cephalosporins

#### Second Generation

**Cefaclor**  
Cecavil  
Ceclobid  
Ceclor/Ceclor CD  
Clorcef  
Clorotir  
Drugmaker's Biotech Cefaclor  
Pharex Cefaclor  
RiteMED Cefaclor  
Verzat/Verzat-ER  
Xelent  
Xeztron  
Zunecar

**Cefotiam**  
Ceradolan

**Cefoxitin**  
Monowel  
Panaxox

**Cefuroxime**  
C-Tri T  
Drugmaker's Biotech Cefuroxime  
Infekor  
Kefsyn  
Panaxim  
Profurex  
RiteMED Cefuroxime  
Rovix  
Xorimax  
Zefur  
Zegen  
Zegen Capsule  
Zinacef  
Zinnat

#### 3rd Generation

**Cefixime**  
Tergececf  
Ultraxime  
Zefral

**Cefotaxime**  
Ceplax  
Cladex  
Clfloran  
Pantaxin

#### 4th Generation

**Cefepime**  
Cepimax

### Macrolides

**Azithromycin**  
Azyth  
Zithromax  
Zmax One Dose

**Clarithromycin**  
Clariget  
Galemin  
Klaricid/Klaricid OD  
Kllarmyn  
Klaz  
Larizin  
Maxulid  
Onexid  
Pharex Clarithromycin

### Erythromycin

**Am-Europharma Erythromycin**  
Drugmaker's Biotech Erythromycin  
Erasymin  
Erythocin/  
Erythocin DS  
Ilosone  
Pharex Erythromycin  
RiteMED Erythromycin  
Upperzin

**Ampicillin**  
Ampicin  
Baclimed  
DLI Ampicillin  
Drugmaker's Biotech Ampicillin  
Eurocin  
Excilllin  
Panacta  
Pentrexyl  
Picaplin  
Polypen  
Vatacill

**Cefoperazone**  
Sulperazone

**Cefpodoxime**  
Banan

**Ceftazidime**  
Fortum  
RiteMED Ceftazidime  
Zeptigen

**Ceftizoxime**  
Unizox

**Ceftriaxone**  
Forgram  
Keptrix  
Megion  
Pantixon  
Retrokor  
RiteMED Ceftriaxone  
Rocephin  
Sergimax  
Xefatrex

**Thromyn**

**Lincomycin**  
Lincoxin

**Penicillins**

**Amoxicillin**  
Amoxil  
Amusa  
Clifam  
Clearamox  
Daisamox  
DLI Amoxicillin  
Drugmaker's Biotech Amoxicillin  
Eleomox  
Globamox  
Globalpen  
Himox  
Lewixin  
Medimoxil  
Megamox  
Moxilllin  
Multicare Amoxicillin  
Novamox  
Pediamox  
Pharex Amoxicillin  
Promox  
RiteMED Amoxicillin  
Sterimox  
Sumoxil  
Teramoxyl  
Valzimox  
Vaxman  
Yugoxil
Community-Acquired Pneumonia

**Benzathine benzylpenicillin**
Zalpen

**Benzylpenicillin potassium**
Ritemed Benzyl Penicillin Potassium

**Benzylpenicillin sodium**
YSS Benzylpenicillin Sodium

**Cloxacillin**
Avastoph
Drugmaker's Biotech Cloxacillin
Encloxil
Lewinex
Medix
Oxaclen
Pannox
Pharex Cloxacillin
Prostaphlin-A
RiteMED Cloxacillin
Secloxin

**Co-Amoxiclav**
Amoclav
Augmentin
Augmex
Bioclavid
Cax
Clavace
Clavoxel
Clovimax
Drugmaker's Biotech Amoxicillin + Clavulanic Acid
Enhamox
Exten
Natravox

**Flucloxacillin**
Drugmaker's Biotech Flucloxacillin
Fluclo
Staffoxin

**Oxacillin**
Prostaphilin
Wydox

**Pen G Benzathine**
Penadur L-A

**Phenoxymethylpenicillin K**
Sumapen

**Sulbactam/Ampicillin**
Unasyn IM/IV

**Sultamicillin**
Unasyn Oral
Zunamyn

**Tazobactam/Piperacillin**
Piptaz
Tazocin

**Ticarcillin sodium/Clavulanate potassium**
Timentin

**Quinolones**

**Ciprofloxacin**
Ciprobay/Ciprobay XR
Cipromax
Cipromet
Cirok
Drugmaker's Biotech Ciprofloxacin
Floxacef
Hyprocel
Ipromax
Pharex Ciprofloxacin
Pharex Ciprofloxacin
Proxazin
Proxivex
Quiprime
Xipro
Zunexan
Zyflor

**Gatifloxacin**
Tequin

**Levofloxacin**
Floxel
Levox
Wilovex

**Moxifloxacin**
Avelox

**Norfloxacin**
Drugmaker's Biotech Norfloxacin
Ellatracid
Euroflox
Lexinor
Pharex Norfloxacin
Urutaric Reformulated
Urobacid
Winatfox

**Ofloxacin**
Baciflox
Drugmaker's Biotech Ofloxacin
Fluraxid
Gyros
Inoflox
Iquinol
Itex
Kelfil
Pharex Ofloxacin
Qiflon
Qinolox

**Pefloxacin**
Floquin

**Rufloxacin HCl**
Uroclar

**Sulfonamide Combinations**

**Cotrimoxazole**
Am-Europharma Cotrimoxazole
Bacidal
Bactille-TS
Bactrim
Bacxal
Chromo-Z
Colimox
Cotribase
DLI-Cotrimoxazole
Drugmaker's Biotech Cotrimoxazole
Globaxol
Katherx
Lagatrim Forte
Lictora
Macromed
Moxzole

**Non-steroidal Anti-inflammatory Drugs (NSAIDs)**

**Benzathine benzylpenicillin**
Zalpen

**Benzylpenicillin potassium**
Ritemed Benzyl Penicillin Potassium

**Benzylpenicillin sodium**
YSS Benzylpenicillin Sodium

**Cloxacillin**
Avastoph
Drugmaker's Biotech Cloxacillin
Encloxil
Lewinex
Medix
Oxaclen
Pannox
Pharex Cloxacillin
Prostaphlin-A
RiteMED Cloxacillin
Secloxin

**Co-Amoxiclav**
Amoclav
Augmentin
Augmex
Bioclavid
Cax
Clavace
Clavoxel
Clovimax
Drugmaker's Biotech Amoxicillin + Clavulanic Acid
Enhamox
Exten
Natravox

**Flucloxacillin**
Drugmaker's Biotech Flucloxacillin
Fluclo
Staffoxin

**Oxacillin**
Prostaphilin
Wydox

**Pen G Benzathine**
Penadur L-A

**Phenoxymethylpenicillin K**
Sumapen

**Sulbactam/Ampicillin**
Unasyn IM/IV

**Sultamicillin**
Unasyn Oral
Zunamyn

**Tazobactam/Piperacillin**
Piptaz
Tazocin

**Ticarcillin sodium/Clavulanate potassium**
Timentin

**Quinolones**

**Ciprofloxacin**
Ciprobay/Ciprobay XR
Cipromax
Cipromet
Cirok
Drugmaker's Biotech Ciprofloxacin
Floxacef
Hyprocel
Ipromax
Pharex Ciprofloxacin
Pharex Ciprofloxacin
Proxazin
Proxivex
Quiprime
Xipro
Zunexan
Zyflor

**Gatifloxacin**
Tequin

**Levofloxacin**
Floxel
Levox
Wilovex

**Moxifloxacin**
Avelox

**Norfloxacin**
Drugmaker's Biotech Norfloxacin
Ellatracid
Euroflox
Lexinor
Pharex Norfloxacin
Urutaric Reformulated
Urobacid
Winatfox

**Ofloxacin**
Baciflox
Drugmaker's Biotech Ofloxacin
Fluraxid
Gyros
Inoflox
Iquinol
Itex
Kelfil
Pharex Ofloxacin
Qiflon
Qinolox

**Pefloxacin**
Floquin

**Rufloxacin HCl**
Uroclar

**Sulfonamide Combinations**

**Cotrimoxazole**
Am-Europharma Cotrimoxazole
Bacidal
Bactille-TS
Bactrim
Bacxal
Chromo-Z
Colimox
Cotribase
DLI-Cotrimoxazole
Drugmaker's Biotech Cotrimoxazole
Globaxol
Katherx
Lagatrim Forte
Lictora
Macromed
Moxzole

**Carbapenems**
Ertaopenem
Invanz
Impenem/Cilastatin
Tienam
Meropenem
Meronem

**Other Antibiotic**
Linezolid
Zyvox

**Antiprotozoals**
Metronidazole
Abbot Metronidazole (Premixed)
Am-Europharma Metronidazole
Anerobia
Drugmaker's Biotech Metronidazole
Flagyl
Metinox
Metaloid
Metrolag
Pharex Metronidazole
Servizol
Tricomycin
Triconex

**Vaccines for Active Immunization**
Hib
Act-Hib
Hiberix*
Infantrix Hexa*
Pentaxim*
Tettract-Hib*
Vaxem Hib

**Influenza**
Fluarix
Vaxigrip

**Other vaccines for Active Immunization**
Broncho-Vaxom
Pneumo 23
Prevenar