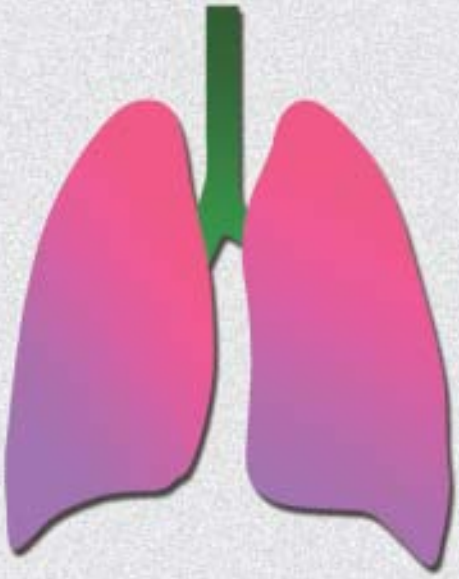
Clinical Practice Guidelines

Community-Acquired Pneumonia

Philippine Clinical Practice Guidelines

Diagnosis, Empiric Management and Prevention of Community-Acquired Pneumonia in Immunocompetent Adults

2004 UPDATE



Joint Statement of PSMID • PCCP • PAFP

Published by Philippine Practice Guidelines Group in Infectious Diseases
(PPGG-ID)

ISBN 971-92130-4-3

This guideline is intended for use by health care professionals including medical specialists, clinical practitioners, nurses, administrators and policy makers.

Citation as to source is suggested in the following format:

Philippine Clinical Practice Guidelines on the
Diagnosis, Empiric Management And Prevention of
Community-acquired Pneumonia in Immunocompetent Adults
2004 Update
Joint Statement of the
Philippine Society for Microbiology & Infectious Diseases
Philippine College of Chest Physicians
Philippine Academy of Family Physicians

Printed by
Zurbano Publishing & Printing Corp.
2195 Primo Rivera Street, Brgy. La Paz
Makati City

PHILIPPINE CLINICAL PRACTICE GUIDELINES ON THE DIAGNOSIS, EMPIRIC MANAGEMENT AND PREVENTION OF COMMUNITY-ACQUIRED PNEUMONIA IN IMMUNOCOMPETENT ADULTS

2004 UPDATE

Joint Statement of PSMID • PCCP • PAFP

TASK FORCE ON COMMUNITY-ACQUIRED PNEUMONIA

Vilma M. Co, MD	PSMID	Chair
Myrna T. Mendoza, MD	PSMID	Co-Chair
Ma. Lourdes A. Villa, MD	PSMID	Rapporteur
Abundio A. Balgos, MD	PCCP	Member
Joselito R. Chavez, MD	PCCP	Member
Jennifer A. Chua, MD	PSMID	Member
Manolito L. Chua, MD	PSMID	Member
Remedios F. Coronel, MD	PSMID	Member
Raquel Victoria M. Ecarma, MD	PSMID	Member
Benilda B. Galvez, MD	PCCP	Member
Manuel C. Jorge, MD	PCCP	Member
Policarpio B. Joves, MD	PAFP	Member
Isaias A. Lanzona, MD	PCCP	Member
Ma. Bella R. Siasoco, MD	PCCP	Member
Maribel B. We, MD	PSMID	Member

Thelma E. Tupasi, MD, FPSMID
Adviser

PANEL OF EXPERTS

PSMID	Angeles Tan-Alora, MD Mediadora C. Saniel, MD Thelma E. Tupasi, MD
PCCP	Roberto A. Barzaga, MD Teresita S. de Guia, MD Camilo C. Roa, Jr., MD
PAFP	Cynthia L. Hipol, MD Zorayda E. Leopando, MD Reynaldo A. Olazo, MD
PCR	Emmanuel D. Almasan, MD

TABLE OF CONTENTS

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 supervene 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 Specialist (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 Eat 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. Afterall, "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 a collaborative undertaking of various medical specialty societies concerned with the care of patients with CAP such as the Philippine Society for Microbiology and Infectious Diseases (PSMID), Inc., Philippine College of Chest Physicians (PCCP), American College of Chest Physicians-Philippine Chapter (ACCP-PC), Philippine Academy of Family Physicians (PAFP), Department of Health (DOH), Philippine College of Radiology (PCR), and the Philippine College of Emergency Medicine and Acute Care (PCEMAC). Inputs from other stakeholders and end-users were also taken into account through discussions and supplemented by questionnaires using the modified Delphi technique.

The recommendations have been based on evidence derived from a critical review of the literature. A systematic search of the literature using computer-based search strategies was first undertaken and relevant articles, including local data, when available, were selected. A Medline search of the medical literature was conducted using combinations of query terms which included community-acquired pneumonia, signs, symptoms, chest radiography, microbiology, sputum Gram's stain and culture, diagnosis, hospitalization, risk

factors, treatment, mortality, outcome, prognosis, prevention, pneumococcal and influenza vaccines. This document is meant for medical specialists in the field of infectious disease, pulmonary, family medicine, and general practitioners involved in the care of CAP in the outpatient and hospital setting.

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 & 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 an acute cough, abnormal vital signs of tachypnea (RR > 20 breaths per minute), tachycardia (CR > 100/min), and fever (T > 37.8ºC) with at lease 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.[1] There is

reported significant inter-observer agreement among physicians in obtaining clinical symptoms and signs in diagnosing patients with possible CAP. [2,3] Patients with atypical pneumonia may present with predominantly extrapulmonary symptoms.[4] Furthermore, elderly patients may not present with the classical symptoms of fever, cough, and dyspnea.[5]

History

Prospective cohort trials evaluated the sensitivity and specificity of the clinical history in pneumonia. [6,7,8,9] 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.[10] 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. [11, 12]

Physical Examination

Vital sign abnormalities on the probability of pneumonia depend on the cut-off value set by studies in defining an abnormal result. [10] A respiratory rate greater than 20 breaths/min resulted in a likelihood ratio of only 1.2 in one study [7] but a respiratory rate greater than 25 breaths/min increased the likelihood ratio to 1.5 to 3.4.[6, 9] 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. [9]

Like the history in Table 1, abnormal lung findings (e.g. crackles) increase the probability of pneumonia by only a small amount.[10] 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. [7]

Table 1. Accuracy of history and physical examination for the diagnosis of community-acquired pneumonia*

Type of Finding**	Positive Likelihood Ratio‡	Negative Likelihood Ratio‡
Medical History		
Fever	1.7 – 2.1	0.6 – 0.7
Chills	1.3 – 1.7	0.7 - 0.9
Vital signs		
Tachypnea¶	1.5 – 3.4	0.8
Tachycardia§	1.6 – 2.3	0.5 – 0.7
Hyperthermia	1.4 – 4.4	0.6 – 0.8
Chest examination		
Dullness to percussion	2.2 – 4.3	0.8 – 0.9
Decreased breath sounds	2.3 – 2.5	0.6 – 0.8
Rhonchi	1.4 – 1.5	0.8 – 0.9
Egophony	2.0 – 8.6	0.8 – 1.0

* Adapted from Metlay et al [10]

** 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/1 – specificity) 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

¶ Tachypnea defined as respiratory rate > 25 breaths /min.

§ Tachycardia defined as heart rate > 100 beats/min in 2 studies and > 120 beats/min in a third study.

Combination of History and Physical Examination

Prediction rules combining history and physical examination significantly affect the probability of pneumonia.[6,8,9] 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.[13] These prediction rules may be utilized to help physicians identify patients who may have pneumonia and therefore need a chest x-ray.

Three studies have proven that combinations of history and physical examination findings significantly affect the probability of pneumonia.[6,8,9] Assuming a baseline prevalence of pneumonia of 5%, a prediction rule may be applied to a patient with an acute cough, fever, tachycardia and crackles. 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 only from 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.

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

Decision Basis	Physician's Clinical Judgment	Heckerling et. al. Score (threshold was 2 points)	Gennis et. al. Rule (threshold was 1 point)
Variables	History Physical findings	• Temperature of > 37.8°C • Pulse of > 100/min • Rales • Decreased breath sounds • Absence of asthma	• Temperature of > 37.8°C • Respiration of > 20/min
Accuracy in in Predicting pneumonia	60%	68%	76%

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

- For diagnostic certainty in the management of a patient with suspected pneumonia, chest radiography should be performed.
- Chest x-ray is also essential in assessing severity of disease & in prognostication.
- It may suggest possible etiology & 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 a 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 my mimic it *(Grade A).*

Summary of evidence:

Physicians' ability to assess community-acquired pneumonia on clinical grounds is low and cannot replace chest radiographs.[14] Consensus statements from professional organizations strongly recommend the need for chest radiography to confirm the diagnosis of community-acquired pneumonia.[1, 15] 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 (Table 3)[18] In a metaanalysis 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]

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

Chest radiographic findings	Odds Ratio	95% C.I.*
Multilobar radiographic pulmonary infiltrate[19]	3.1	1.9 – 5.1
Bilateral pleural effusion[19]	2.8	1.4 – 5.8

**Confidence Interval*

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 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 (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 (see page 18).

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 be aggravate or be aggravated by the pneumonia are included in this category. These patients **need to be hospitalized for parenteral therapy** *(Grade A)*.

Table 4. Clinical features of patients with CAP according to risk categories

Low Risk CAP	Moderate Risk CAP	High Risk CAP
Stable vital signs • RR < 30 breaths/min • PR < 125 beats/min • SBP > 90 mmHg • DBP > 60 mmHg **No or stable comorbid conditions** **No evidence of extrapulmonary sepsis** **No evidence of aspiration** **Chest X-ray:** • localized infiltrates • no evidence of pleural effusion nor abscess • not progressive within 24 hrs	**Unstable vital signs**: • RR > 30 breaths/min • PR > 125 beats/min • Temp > 40°C or <35°C **Unstable comorbid condition** *(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)* **Evidence of extrapulmonary sepsis** (hepatic, hematologic, gastrointestinal, endocrine) **Suspected aspiration** **Chest X-ray:** • multilobar infiltrates • pleural effusion or abscess • progression of findings to > 50% in 24 hrs	**Any of the clinical feature of moderate risk CAP plus any of the following:** 1. Shock or signs of hypoperfusion • hypotension • altered mental state • urine output < 30 ml/hr 2. Hypoxia (PaO_2 < 60 mmHg) or Acute hypercapnea ($PaCO_2$ > 50 mmHg) **Chest X-ray:** • as in moderate risk CAP

High Risk CAP

Patients with impending or frank respiratory failure (i.e. hypoxemia with PaO2 <60 mmHg or acute hypercapnea with PaCO2 >50 mmHg) 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.[20] It has also been shown that when making a decision about hospitalization for 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. [21]

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 in over-all bed-days per patient without any increase in deaths, complications, use of the intensive care unit, or re-admissions or any decrement in the health-related quality of life. [22,,23,24,25,26] *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.*[27] *A study by Halm et al*[28] *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.*

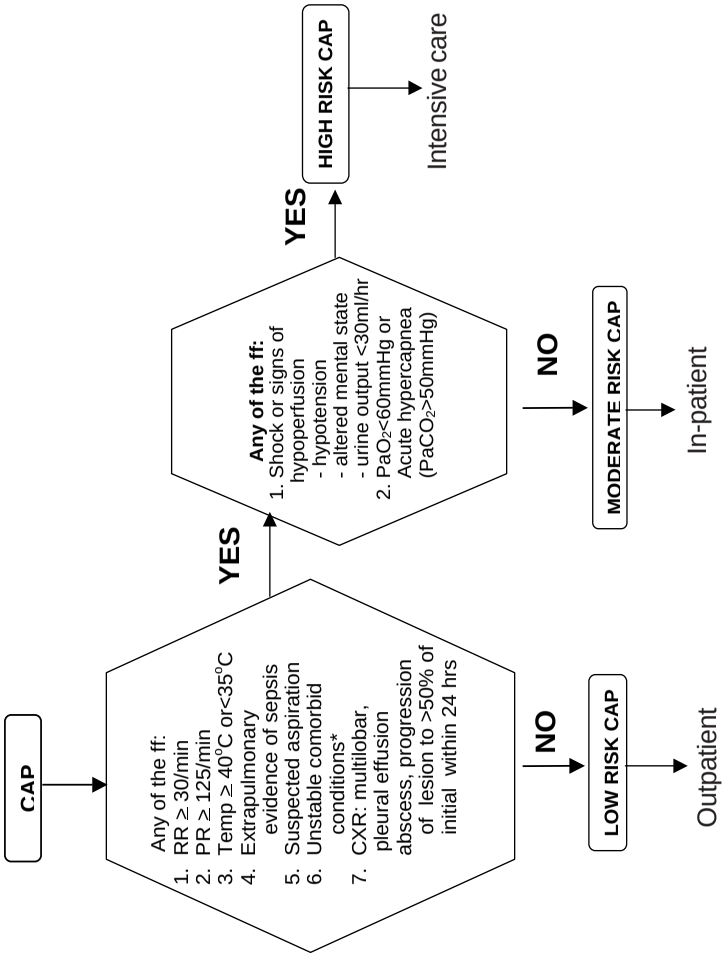


Figure 1. **Algorithm for the management-oriented risk stratification of community-acquired pneumonia (CAP) in immunocompetent Adults**

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.[29] 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.[1]

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. [15] 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 mm Hg at room air), and radiographic findings of pleural effusion are independently associated with increased mortality. [1]

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 Hemophilus 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, Chlamydophilia 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 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.[30, 31]

Summary of evidence:

- *Definite etiology: The etiologic diagnosis is considered definite when the pathogen is isolated from uncontaminated 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.*[1]

• *Probable etiology: Pathogens demonstrated by smear or culture isolated in moderate to heavy quantity from respiratory secretions (expectorated sputum, bronchoscopic aspirate, quantitatively cultured bronchoalveolar lavage fluid or brush catheter specimen) are considered probable etiology. Although with some limitations, gram stain and culture when done on expectorated sputum of good quality (PMN>25, squamous cells <10/ low power field) reflect cultures of transtracheal aspirate and provide good information. A physician aided by the predominant morphology from gram-stained sputum could theoretically select the appropriate monotherapy in approximately 94% of the time.[32] The sputum specimen should be rapidly transported and processed in the laboratory within 1 to 2 hours of collection.[1]*

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/oil immersion field predicted the blood isolate in 67.7% of the time. This increased to 89.5% in patients with concentration of >10/oil immersion field.[33] Another study by Rein revealed a Gram stain sensitivity of 62% and a specificity of 85% in identifying pneumococci in sputum.[34]

Cultures of expectorated sputum are more difficult to interpret. These may be contaminated with resident flora of the upper airways which may be potential pathogens thus leading to false positive results. They are not sensitive in patients who have taken previous antibiotics, in those unable to expectorate and in those with delays in the processing of the specimens. Nevertheless, cultures of appropriate specimens may be clinically significant. S. pneumoniae was isolated in the sputum in 64% (29/45) of patients with presumed pneumococcal pneumonia based on the finding of Gram positive diplococci compared to 6% (2/31) of patients without Gram positive diplococci.[35]

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. [34,36,37]

A specific etiologic agent is isolated in only 40-60% of cutures done.[1] An outpatient study in the Philippines showed that among 197 patients, H. influenzae (19%) and S. pneumoniae (11%) were still the predominant

etiologic agents. Atypical pathogens (M. pneumoniae, C. pneumoniae and Legionella sp) were seen in 6% of the patients.[38] Local prevalence data in 2003 [39] has identified atypical pathogens as occuring in 43% of samples in hospitalized patients. They occured 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 (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.

Table 5. Diagnostic tests for *M. pneumoniae, C. pneumoniae*, and *L. pneumophila*

Test	Sensitivity	Specificity
Diagnostic tests for *M. pneumoniae*[40]		
Respiratory or Tissue Culture	>90	50-90
Serology (Complement Fixation, ELISA)	75-80	80-90
PCR	95	95-99
Diagnostic tests for *C. pneumoniae* [40,41]		
Respiratory or Tissue Culture	50-90	?
Serology (Microimmunofluorescence)	50-90	>85
PCR	>90	>90
Diagnostic tests for *L. pneumophila* [40,42]		
Sputum Culture	75-99	100
Serology	40-75	95
Urine antigen	60-70	99
PCR	>90	>90
Direct Fluorescent Antibody Test (DFA)	25-75	>90

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 (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[38]. 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 pneumonias, the pattern of extrapulmonary involvement is highly characteristic for atypical organisms such as *Mycoplasma pneumoniae* and *Chlamydophilia 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, sultamicillin, the second-generation oral cephalosporins (i.e., cefuroxime axetil, or cefaclor), or the extended macrolides or azalides are recommended *(Grade A)*. For patients with hypersensitivity to beta-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 nonpseudomonal beta-lactam with or without a beta-lactamase inhibitor in

Table 6: Empiric antimicrobial therapy in CAP

Risk Stratification	Potential Pathogen	Empiric Therapy
Low Risk CAP	*Streptococcus pneumoniae* *Haemophilus influenzae* *Chlamydophilia pneumoniae* *Mycoplasma pneumoniae* *Moraxella catarrhalis* Enteric Gram-negative bacilli (among those with co-morbid illness)	**Previously healthy:** amoxicillin **OR** extended macrolides Alternative: cotrimoxazole **With stable comorbid illness:** co-amoxiclav **OR s**ultamicillin **OR** 2nd generation cephalosporins **OR** extended macrolides
Moderate Risk CAP	*Streptococcus pneumoniae* *Haemophilus influenzae* *Chlamydophilia pneumoniae* *Mycoplasma pneumoniae* *Moraxella catarrhalis* Enteric Gram-negative bacilli *Legionella pneumophila* Anaerobes (among those with risk of aspiration)	IV nonpseudomonal b-lactam with or without b-lactamase inhibitor + macrolide **OR** antipneumococcal fluoroquinolones (FQ)
High Risk CAP	*Streptococcus pneumoniae* *Haemophilus influenzae* *Chlamydophilia pneumoniae* *Mycoplasma pneumoniae* *Moraxella catarrhalis* Enteric Gram-negative bacilli *Legionella pneumophila* Anaerobes (among those with risk of aspiration) *Staphylococcus aureus* *Pseudomonas aeruginosa*	**No risk for *P. aeruginosa*:** a. IV nonpseudomonal b-lactam with or without b-lactamase inhibitor + IV macrolide b. IV antipneumococcal FQ **With risk for *P. aeruginosa:*** IV pseudomonal b-lactam with or without b-lactamase inhibitor + IV macrolide or IV antipneumococcal FQ +/- aminoglycoside or IV ciprofloxacin

Table 7. Usual recommended dosages of antibiotics in 50-60 KBW adults with normal liver and renal functions

Antibiotic	Dosage	Antibiotic	Dosage
Low Risk CAP *(all taken orally)*			
B-lactams:		*β-lactams w/ β-lactamase inhibitor:*	
Amoxicillin	500 mg TID	Co-amoxiclav	625 mg TID or 1 gm BID
Trim/sulfonamide:	160/800 mg	Sultamicillin	750 mg BID
Cotrimoxazole	BID		
Macrolides		*2nd gen. cephalosporins*	
Azithromycin	500 mg OD	Cefuroxime axetil	500 mg BID
Clarithromycin	500 mg BID	Cefaclor	500 mg TID or
Roxithromycin	150 mg BID or 300 mg OD		750 mg BID
Moderate Risk CAP			
Macrolides		*2nd gen. cephalosporins*	
Erythromycin IV	0.5 - 1 g q 6h	Cefotiam IV	1g q 8 h
Azithromycin PO or IV	500 mg q 24 h	Cefuroxime IV	1.5 g q 8 h
Clarithromycin PO or IV	500 mg q 12 h	Cefoxitin IV (with	1-2 g q 8 h
Roxithromycin P O	150 - 300 mg BID	anaerobic activity)	
Antipneumococcal Fluoroquinolones		*3rd gen. cephalosporins*	
Levofloxacin PO or IV	500 mg q 24 h	Ceftriaxone IV	1-2 g q 24 h
Gatifloxacin PO or IV	400 mg q 24 h	Cefotaxime IV	1-2 g q 8 h
Moxifloxacin PO or IV	400 mg q 24 h	Ceftizoxime IV (with anaerobic activity)	1-2 g q 8h
b-lactams w/ b-lactamase inhibitor:		*Carbapenem*	
Sulbactam-Ampicillin IV	1.5 g q 8 h	Ertapenem IV (with	1 g q 24 h
Coamoxiclav IV	1.2 g q 8 h	anaerobic activity)	
High Risk CAP *(all routes are intravenous)*			
Macrolides		*3rd gen. cephalosporins*	
Erythromycin	0.5-1 g q 6h	Ceftriaxone	1-2 g q 24 h
Azithromycin	500 mg q 24 h	Cefotaxime	1-2 g q 8 h
Clarithromycin	500 mg q 12 h	Ceftizoxime	1-2 g q 8 h
Fluoroquinolones			
Levofloxacin	500 mg q 24 h	*Carbapenem*	
Gatifloxacin	400 mg q 24 h	Ertapenem	1 g q 24 h
Moxifloxacin	400 mg q 24 h		
Ciprofloxacin	400 mg q 12 h	*Anti-pseudomonal β-lactams*:	
Aminoglycosides		Ceftazidime	2 g q 8 h
Amikacin	15 mg/kg q 24h	Cefepime	2 g q 8-12 h
Gentamicin	3 mg/kg q 24 h	Cefpirome	2 g q 12 h
Netilmicin	7 mg/kg OD	Ticarcillin-Clavulanate	3.2 g q 6 h
Tobramycin	3 mg/kg q 24 h	Piperacillin-Tazobactam	2.25-4.5 g q 6- 8 h
		Sulbactam-cefoperazone	1.5 g q 12
b-lactams w/ b-lactamase inhibitor:		Imipenem	500 mg q 6 h
		Meropenem	1-2 g q 8 h
Sulbactam-Ampicillin	1.5 g q 6-8 h		
Co-amoxiclav	1.2 g q 6-8 h	*Others:*	
		Oxacillin	1- 2 g q 4-6 h
		Clindamycin	600 mg q 8 h
		Metronidazole	500 mg q 6-8 h

addition to a macrolide is recommended. Parenteral nonpseudomonal beta-lactams include cephalosporins such as cefuroxime sodium, ceftriaxone or cefotaxime. Cefoxitin, ceftizoxime or ertapenem are options which also have anaerobic activity *(Grade A)*. Agents which combine a beta-lactam with beta-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 above regimens with macrolides is now recommended as a significant prevalence of *Legionella* was noted among hospitalized patients in a recent local study. An alternative regimen for moderate-risk CAP includes the use of antipneumococal fluoroquinolones alone *(Grade A)*. Although the newer anti-pneumococcal quinolones such as levofloxacin, gatifloxacin or moxifloxacin are also options for therapy, it is recommended that they be reserved as potential second line agents for the treatment of pulmonary tuberculosis, particularly for multi-drug resistant tuberculosis *(Grade C)*. For suspected aspiration especially in those with depressed sensorium or seizure episodes, choose a beta-lactam with anaerobic activity or add clindamycin or metronidazole to the regimen.

HIGH RISK CAP: Empiric coverage for patients at high risk of morality 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 beta-lactam with or without a beta- lactamase inhibitor (b) a parenteral macrolide or antipneumococcal fluoroquinolone with or without (c) aminoglycoside or parenteral ciprofloxacin *(Grade A)*. Anti-pseudomonal beta-lactams include ceftazidime, cefepime or cefpirome. Carbapenems such as Meropenem or Imipenem-cilastatin have anaerobic activity. Parenteral antipseudomonal beta-lactams with beta-lactamase inhibitors include piperacillin-tazobactam, ticarcillin-clavulanic acid and sulbactam-cefoperazone.

Staphylococcus. In patients shown or suspected to have lung abscesses, pneumatocoeles 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.[43] Among patients hospitalized for CAP, antibiotic therapy should be initiated within 4 hours after diagnosis has been made. [41,44,45,46,47] 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.

Table 8. Rank order of etiologic agents of CAP

Rank	1st	2nd	3rd	4th	5th
			OUTPATIENTS		
Philippines [37]	*H.influenzae*	*S. pneumoniae*	*S.pneumoniae* *+H.influenzae*	*H. influenzae* *+ Moraxella sp* *+ C. pneumoniae*	—
Sweden [48]	*S. pneumoniae*	*H.influenzae*	*M.pneumoniae*	Viruses	*C.pneumoniae*
Thailand [49]	*C.pneumoniae*	*M.pneumoniae*	*S. pneumoniae*	mixed	*L. pneumophila*
US [50]	*H. influenzae*	*S. pneumoniae*	*M. catarrhalis*	—	—
Spain [51]	*S. pneumoniae*	*M.pneumoniae*	*C.pneumoniae*	—	—
Lausanne [52]	*S. pneumoniae*	*M.pneumoniae*	*C.pneumoniae*	*C. burnetii*	*H. spp.*
Finland [53]	*S. pneumoniae*	*C.pneumoniae*	*M.pneumoniae*	Viruses	*H. Influence*
Slovenia [54]	*M. pneumoniae*	*C. pneumoniae*	*S. pneumoniae*	mixed	—
			IN-PATIENTS		
Philippines [55]	*G(-) bacilli*	*S. pneumoniae*	*M. catarrhalis*	—	—
Philippines [31]	*S. pneumoniae*	*M.tuberculosis*	*Chlamydia spp*	*L. pneumophila*	*M.pneumoniae*
Thailand [49]	*S. pneumoniae*	G(-)bacilli	*C.pneumoniae*	*M. pneumoniae*	mixed
Spain [56]	*S. pneumoniae*	*H.influenzae*	—	—	—
Japan [57, 58]	*S. pneumoniae*	*H.influenzae*	*M.pneumoniae*	*C. pneumoniae*	*S. milleri grp.*
Japan [59]	*S. pneumoniae*	*H.influenzae*	*M.pneumoniae*	*C. pneumoniae*	*S. aureus*
Japan [60]	*S. pneumoniae*	*H.influenzae*	*C.pneumoniae*	*M. pneumoniae*	Viruses
Korea [61]	*S. pneumoniae*	*K.pneumoniae*	*C.pneumoniae*	*P. aeruginosa*	*S. aureus*
Malaysia [62]	*K.pneumoniae*	*S. pneumoniae*	*H. influenzae*	*M. pneumoniae*	*P. aeruginosa*
Malaysia [63]	*M. tuberculosis*	*K.pneumoniae*	*P. aeruginosa*	*S. aureus*	*S. pneumoniae*
US [64]	*S. pneumoniae*	G(-)bacilli	*Legionella*	*H.i influenzae*	*S. aureus*
Israel [65]	*S. pneumoniae*	*S. aureus*	*H. influenzae*	—	—
U. Kingdom [66]	*S. pneumoniae*	Viruses	*C.pneumoniae*	*H. influenzae*	*M. pneumoniae*

The Antimicrobial Resistance Surveillance Program (ARSP)[67] 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. pneumonia 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.

Table 9. Resistance rates of *S. pneumoniae* (ARSP, 1999 - 2003)

	Penicillin	Cotrimoxazole	Chloramphenicol	Erythromycin
1999	5	7	3	-
2000	18	12	7	-
2001	9	10	3	-
2002	6	9	3	-
2003	9.2	9.1	2.9	2.3

Table 10. Resistance rates of *H. influenzae* (ARSP, 1999 - 2003)

	Cotrimoxazole	Ampicillin	Chlorampenicol	Clarithromycin	Azithromycin
1999	7	10	3	-	-
2000	11	3	4	-	-
2001	16	6	0	-	-
2002	11	5	5	-	-
2003	18	13	11.8	0	1.4

Most of these studies (Table 8) demonstrate the presence of the atypical pathogens. Macrolides and azalides provide coverage against these potential pathogens. Woodhead [68] as well as Mundy et. al [69] 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.[15,70] Other regimens such as co-amoxiclav, sultamicillin, 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 Philippines[75] 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. tb to qunolones 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.[39] *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 beta-lactam agents which are also effective against Gram-negative bacilli.*[78-85] *Parenteral erythromycin is the standard regimen for severe Legionella pneumonia. The extended macrolides may be given orally alongside parenteral beta-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.
- 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 (Table 11). *(Grade C)*

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

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

Antibiotic	Dosage	Antibiotic	Dosage
Cefprozil	500 mgs BID	Co-amoxiclav	1 gm BID
Cefuroxime	500 mg BID	Sultamicillin	750 mgs BID
Cefaclor	500 mg TID or 750 mg BID	Azithromycin	500 mg OD
		Clarithromycin	500 mg BID
Ceftibuten	400 mgs OD	Levofloxacin	500 mg OD
Cefixime	100-200 mg BID	Gatifloxacin	400 mg OD
Cefpodoxime	100-200 mgs BID	Moxifloxacin	400 mg OD

*in adults, 50-60 KBW with normal liver and renal 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 treatment should be prolonged to 10-14 days. A 2-week period of therapy is recommended for *Mycoplasma* and *Chlamydophilia* while *Legionella* is treated for 14-21 days. A 3-day course of oral therapy for low-risk CAP is possible with new agents such as the azalides which possess pharmacodynamic characteristics prolonging their duration of effect.(Table 13)

Table 13. Duration of antibiotic use based on etiology

Etiologic Agent	Duration of therapy (days)
• Most bacterial pneumonia except enteric gram (-) pathogens, *S. aureus*, and *P. aeruginosa*	5-10 3 (azalides) for *S. pneumoniae*
• Enteric gram (-) pathogens, *S. aureus*, and *P. aeruginosa*	14
• Mycoplasma and Chlamydophilia	10-14
Legionella	14-21

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 coexisting illness or other life-threatening complication, the patient may be discharged once clinical stability occurs and oral therapy is initiated. (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. [104]

Table 14. Recommended hospital discharge criteria

During the 24 hours before discharge, the patient should have the following characteristics (unless this represents the baseline status):

1. temperature of 36-37.5 ^{O} C
2. pulse < 100/min
3. respiratory rate between 16-24/minute
4. systolic BP >90 mmHg
5. blood oxygen saturation >90%
6. with a functioning gastrointestinal tract

***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 to defervescense.[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.[106] 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 an 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.[19,107]

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 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 judgement

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 leukocyte 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]

Table 15. Benefits of intravenous to oral sequential antibacterial therapy

Benefits for patients
More convenient
Less local adverse effects related to intravenous administration, such as phlebitis
Earlier mobilization- lower risk of thrombosis
Reduced hospital stay- lower risk for cross or nosocomial infections
Pharmacoeconomic benefits
Less infusion equipment, cannula and infusion bottles required
Less hospital waste to dispose of
Oral antibacterials less expensive than parenteral antibacterials
Reduced storage costs for parenteral therapy
Less hospital staff time required
Reduced length of hospital stay

In hospitalized patients with CAP without clinical indications of meninigitis 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 MIC_{50} for many common pathogens responsible for CAP. [113,119,120] The improved bioavailability of many new antibiotics allows oral preparations to rapidly achieve adequate serum levels (in patients with a functioning gastrointestinal tract).[121] 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 a superinfection. In such situations, microbiologic studies including blood cultures should be repeated . Unusual pathogens such as M. tuberculosis[31] may be the cause of treatment failure. Special stains of lower respiratory secretions for M. tuberculosis, atypical mycobacteria, 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 unrecognized 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 3 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, 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 M. pneumoniae and 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 (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 *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 (Table 16) : (a) persons > 60 years old (*Grade B*); (b) those with certain chronic illnesses such as cardiovascular disease, lung disease, diabetes mellitus (*Grade A*) ; alcohol abuse, chronic liver disease, CSF leaks (*Grade B*) ; functional or anatomic asplenia (*Grade A*) ; (c) those with immune system disorders such as nephrotic syndrome, HIV infection, hematologic malignancy, generalized malignancies, long-term use of immunosuppressive medications, organ or bone marrow recipients (*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 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

TABLE 16 : Recommendations for pneumococcal vaccination

Indications
- Persons aged > 60 yrs
- 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
- Immunosuppression: HIV, congenital immunodeficiency, malignancies, organ or bone marrow transplantation, chemotherapy, long-term systemic corticosteroids
- Residents of nursing homes & other long-term care facilities

Adult Dose

0.5ml IM or SC (one-time revaccination may be given after 5 years)

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

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]

B. Influenza Vaccine

Influenza vaccine is recommended for any person who are at increased risk for complications from influenza (see Table17). High risk persons for whom influenza vaccination include the following : (a) persons aged > 50 years, (b) those with chronic illnesses (such as lung diseases, cardiovascular diseases, diabetes mellitus, renal dysfunction, hemoglobinopathies) ; (c) immune system disorders (such as 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*)

TABLE 17 : Recommendations for influenza vaccination

Indications

- Persons aged > 50 yrs
- Chronic Illness : chronic pulmonary disease (COPD, asthma, bronchiectasis, chronic PTB) , chronic cardiovascular disease, metabolic diseases (diabetes mellitus), renal dysfunction, hemoglobinopathies
- Immunosuppression : HIV, malignancies, immunosuppressive drugs, radiation therapy, organ or bone marrow transplantation
- Residents of nursing homes & other chronic care facilities
- Pregnant women on their 2nd or 3rd trimester who have not received the flu vaccine w/in the last 12 months
- Health care workers & other personnel of outpatient care settings, hospitals, nursing homes, and chronic care facilities
- Household contacts (including children) & caregivers of persons w/ medical conditions
- Persons who provide essential & emergency community services (policemen, firemen, disaster & relief workers)
- Students & other persons in institutional settings (military, prisons, dormitories)
- Any person who desires to reduce the likelihood of becoming ill with influenza

Adult Dose

0.5 ml IM once a year

Precautions /Contraindications

- Allergy to eggs or to a vaccine component
- Moderate or severe acute illness
- Guillain-Barre Syndrome

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.

IIn 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 aimed at reducing the number of pneumonia cases caused by influenza to lower the possibility of misdiagnosing influenza as SARS. The influenza vaccine does not prevent other respiratory diseases and, importantly, it does not provide protection from SARS.[140]

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.[141] 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. [136]

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.[133]

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. [142,143]

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. [133]

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.[132]

Postlicensure epidemiologic studies have documented the vaccine's efficacy in preventing invasive pneumococcal disease among the elderly and individuals with certain chronic medical conditions. [144] *Only one case-control study failed to demostrate effectiveness against bacteremic disease.,*[145] *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

1. Bartlett JG, Dowell SF, Mandell LA, File TM, Musher DM, Fine MJ. Practice Guidelines for the Management of Community-acquired Pneumonia in adults. Infectious Disease Society of America. Clin Infect Dis 2000; 31:347-82.
2. Wipf JE, Lipsky BA, Hirschmann JV, et al. Diagnosing pneumonia by physical examination: relevant or relic? Arch Intern Med 1999; 159: 1082-7.
3. Metlay JP, Kapoor WN, Fine MJ. Does this patient have community-acquired pneumonia? Diagnosing pneumonia by history and physical examination. JAMA 1997; 278: 1440-5.
4. Cunha BA, Ortega AM. Atypical pneumonia: extrapulmonary clues guide the way to diagnosis. Postgraduate Medicine 1996; 99 (10): 123-132.
5. Metlay JP, Schulz R, Li YH, et al. Influence of age on symptoms at presentation in patients with community-acquired pneumonia. Arch Intern Med 1997; 157: 1453-9.
6. Diehr P, Wood RW, Bushyhead J, Krueger L, Wolcott B, Tompkins RK. Prediction of pneumonia in outpatients with acute cough: a statistical approach. J Chronic Dis 1984; 37: 215-225.
7. Gennis P, Gallagher J, Falvo C, Baker S, Than W. Clinical criteria for the detection of pneumonia in adults: guidelines for ordering chest roentgenograms in the emergency department. J Emerg Med 1989; 7: 263-268.
8. Singal BM, Hodges JR, Radack KL. Decision rules and clinical prediction of pneumonia: evaluation of low-yield criteria. Ann Emerg Med 1989; 18: 13-20.
9. Heckerling PS, Tape TG, Wigton RS, et al. Clinical prediction rule for pulmonary infiltrates. Ann Intern Med 1990: 113: 664-670.
10. Metlay JP, Fine MJ. Testing strategies in the initial management of patients with community-acquired pneumonia. Ann Intern Med 2003; 138: 109-118.
11. Sackett DL. A primer on the precision and accuracy of the clinical examination. JAMA 1992; 267 (19): 2638-2644.
12. Jaeschke R, Guyatt G, Sackett DL. Users' guides to the medical literature. III. How to use an article about a diagnostic test. B. What are the results and will they help me in caring for my patients? The Evidence-based medicine Working Group. JAMA 1994; 271: 703-7.
13. Emerman CL, Damson N, Spore T, et al. Comparison of physician judgment and decision aids for ordering chest radiographs for pneumonia in outpatients. Ann of Emerg Med 1991;20 (11): 1215-1219.
14. Lieberman D, Shvartzman P, Korsonsky I, Lieberman D. Diagnosis of ambulatory community-acquired pneumonia comparison of clinical assessment versus chest x-ray. Scand J Prim Health Care 2003; 21: 57-60.
15. Niederman MS, Mandell LA, Anzueto A, et. al. American Thoracic Society Guidelines for the management of adults with community-acquired pneumonia. Diagnosis, assessment of severity, antimicrobial therapy, and prevention. Am J Respir Crit Care Med 2001; 163: 1730-1754.

16. Macfarlane JT. Lower respiratory tract infection and pneumonia in the community. Semin Respir Infect 1999; 14: 151-162.
17. Albaum N, Hill L, Murphy M, et al. Interobserver reliability of chest radiograph in community-acquired pneumonia. Chest 1996; 110: 343-350.
18. Torres A, Serra-Batlles J, Ferrer A, et al. Severe community-acquired pneumonia. Epidemiology and prognostic factors. Am Rev Respir Dis 1991; 144: 312-318.
19. Fine MJ, Smith MA, Carson CA, et al. Prognosis and outcomes of patients with community-acquired pneumonia: a meta-analysis. JAMA 1996; 275(2): 134-140.
20. Fine MJ, Smith DN, Singer DE. Hospitalization decision in patients with community-acquired pneumonia: a prospective cohort study. Am J Med 1990;89:713-21.
21. Fine MJ, Hough LJ, Medsger AR, et al. The hospital admission decision for patients with community-acquired pneumonia. Arch Intern Med 1997;157:36-44.
22. Marrie TJ, Lau CY, Wheeler SL, Wong CJ, Vandervoort MK, Feagan BG. A controlled trial of a critical pathway for treatment of community-acquired pneumonia. JAMA 2000;283:749-755
23. Atlas SJ, Benzer TI, Borowsky LH, et al. Safely increasing the proportion of patients with community-acquired pneumonia treated as outpatients: an interventional trial. Arch Intern Med 1998;158:1350-1356
24. Dean NC, Suchyta MR, Bateman KA, Aronsky D, Hadlock CJ. Implementation of admission decision support for community-acquired pneumonia. Chest 2000;117:1368-1377
25. Suchyta MR, Dean NC, Narus S, Hadlock CJ. Effects of a practice guideline for community-acquired pneumonia in an outpatient setting. Am J Med 2001;110:306-309.
26. Auble TE, Yealy DM, Fine MJ. Assessing prognosis and selecting an initial site of care for adults with community-acquired pneumonia. Infect Dis Clin North Am 1998;12:741-759.
27. Fine MJ, Auble TE, Yealy DM, et al. A prediction rule to identify low-risk patients with community-acquired pneumonia. N Engl J Med 1997;336:243-250.
28. Halm EA, Atlas SJ, Borowsky LH, et al. Understanding physician adherence with a pneumonia practice guideline: effects of patient, system, and physician factors. Arch Intern Med 2000;160:98-104.
29. Minohue MF, Coley CM, Fine MJ, et al. Patients hospitalized after initial outpatient treatment for community-acquired pneumonia. Ann Emerg Med 1998;21(3):276-380.
30. Interim Clinical Guidelines on SARS for Health Facilities in the Philippines Department Of Health Technical Working group on SARS Clinical Guidelines; 2003.
31. Bernas GA, Galvez BB. Community-Acquired Pneumonia: etiology, clinical profile and outcome. Phil J of Chest Dis 1997; 5(1):31-9.

32. Murray P, Washington J. Microscopic and bacteriologic analysis of expectorated sputum. Mayo Clin Proc. 1975; 50: 339-444.
33. Glekman R, De Vita J, Hibert D, et al. Sputum Gram's stain assessment in bacteremic community acquired pneumonia. J Clin Micro 1988; 26 (3): 846-849.
34. Rein M, Gwaltney J, O'Brien W, et al. Accuracy of Gram's stain in identifying pneumococci in sputum. JAMA, 1982: 247 (5): 642-645.
35. Boerner D, Zwadyk P. The value of sputum Gram's stain in community acquired pneumonia. JAMA, 1982; 247 (5): 642-645.
36. Thorsteinsson S, Musher D, Fagan T. The diagnostic value of sputum culture in acute pneumonia. JAMA 1975; 233 (8): 894-895.
37. Davidson M, Tempest B, Palmer D. Bacteriologic diagnosis of acute pneumonia. Comparison of sputum, transtracheal aspirates and lung aspirates. JAMA 1976; 235(2): 158-163.
38. Taguinod-de los Reyes, MC, Mendoza, MT, Saniel, MC. Open-Labeled Randomized Controlled Trial and Economic Evaluation of Azithromycin in the Outpatient Treatment of Community Acquired Pneumonia in Adults. Dept.of Infectious Disease, UP PGH, 1998 (Unpublished).
39. Saniel MC, Alejandria MM, Ecarma RM et al. Prevalence of atypical pathogens in hospitalized patients with community acquired pneumonia in the Philippines, 2002. (unpublished).
40. File TM, Tan JS, Pflouffe, JE. Lower Respiratory Tract Infections: The role of atypical pathogens: Mycoplasma pneumoniae, Chlamydia pneumoniae and Legionella pneumophila in respiratory infection. Infect Dis Clin of North Am 1998 (12): 3.
41. Mandell LA, Bartlett JG, Dowell SF et al. Update of practice guidelines for the management of community acquired pneumonia in immunocompetent adults. Clin Infect Dis. 2003: 37: 1405-33.
42. Stout JE, Yu V. Legionellosis. New England J Med 1997; 337: 682-687.
43. Moran GJ. New Directions in Antiinfective Therapy for Community-Acquired Pneumonia in the Emergency Department. Pharmacotherapy 2001; 21(7s):95-99.
44. Houck P, Bratzler D, Nsa W, Ma A, Bartlett J. Timing of Antibiotic Administration and Outcomes for Medicare Patients Hospitalized with Community-Acquired Pneumonia. Arch Intern Med 2004; 164:637-44.
45. Chu LA, Bratzer DW, Lewis RJ, et al. Improving the Quality of Care for patients in very small hospitals. Arch Intern Med 2003; 163(3):326-32.
46. Battleman D, Callahan M, Thaler H. Rapid Antibiotic Delivery and Appropriate Antibiotic Selection Reduce Length of Hospital Stay of patients with Community-Acquired Pneumonia: Link between Quality of Care and Resource Utilization. Arch Intern Med 2002, 162(6): 682-8.
47. Natwani D , Williams F, Winter J, Orgston S, Davey P. Use of Indicators to Evaluate the Quality of Community-Acquired Pneumonia management. Clin Infect Dis 2002; 34(3):318-23.

48. Lagerstrom F, Bader M, Foldevi M, Fredlund H, Nordin I, Holmberg H. Microbiological etiology in clinically diagnosed CAP in primary care in Orebro, Sweden. Clin Microbiol Infect 2003; 9(7): 645-52.

49. Wattanathum A, Chaoprasong C, Nunthapisud P, et al. Community-Acquired Pneumonia in Southeast Asia: the microbial differences between ambulatory and hospitalized patients. Chest 2003; 123 (5): 1512-9.

50. Gotfried MH. Epidemiology of clinically diagnosed Community-Acquired Pneumonia in the primary care setting: results from the 1999-2000 respiratory surveillance program. Am J Med *2001*; 111 Suppl 9A: 25S-29S; discussion 36S-38S.

51. Falguera M, Sacristan O, Nogues A, et al. Non-severe Community-Acquired Pneumonia: correlation between cause and severity of co-morbidity. Arch Intern Med 2001;161(15):1866-72.

52. Bochud PY, Moser F, Erard P, et al. Community-Acquired Pneumonia. A prospective outpatient study. Medicine (Baltimore) 2001; 80 (2): 75-87.

53. Jokinen C,Heiskanen L, Juvonen H, et al. Microbial etiology of Community-Acquired Pneumonia in the adult population of 4 municipalities in eastern Finland. Clin Infect Dis 2001; 32(8): 1141-54

54. Beovic B, Bonac B, Kese D, et al. Aetiology and Clinical presentation of mild community-acquired bacterial pneumonia. Eur J Clin Microbiol Infect Dis 2003; 22(10):584-91.

55. San Diego D, Galvez B, Balanag V, Naval S. Philippine Clinical Practice Guidelines of High Risk Community-Acquired Pneumonia: a Surveillance Study, 2001 (unpublished)

56. Zalacain R, Torres A, Celis R, et al. Community-Acquired Pneumonia in the elderly: Spanish multicentre study. Eur Respir J. 2003; 21(2): 294-302.

57. Ishida T, Hashimoto T, Arita M, Ito I, Osawa M. Etiology of Community-Acquired Pneumonia in hospitalized patients: a 3 year prospective study in Japan. Chest 1998; 114:1588-93.

58. Ishida T. Etiology of respiratory infections. Antibiot Chemother 2000; 16:1023-8.

59. Miyashita N, Fukano H, Niki Y, Matsushima T, Okimoto N. Etiology of Community-Acquired Pneumonia requiring hospitalization in Japan. Chest 2000; 119: 1295-6.

60. Matsushima T, Miyashita N, File T. Etiology and management of Community-Acquired Pneumonia in Asia. Curr Opin Infect Dis 2002.15(2): 157-62.

61. Woo JH, Kang J, Kim Y,et al. A prospective multicenter study of Community-Acquired Pneumonia in adults with emphasis on bacterial etiology. Korean J Infect Dis 2001; 33: 1-7.

62. Liam CK, Lim K, Wong C. Community-Acquired Pneumonia in patients requiring hospitalization. Respirology 2001; 6: 259-64.

63. Hooi LN, Looi I, Ng AJ. A study on Community-Acquired Pneumonia in adults requiring hospital admission in Penang. Med J Malaysia 2001; 56(3):275-84.

64. El-Solh A, Sikka P, Ramadan F, Davies J. Etiology of severe pneumonia in the very elderly. Am J Respir Crit Care Med 2001 163: 645-51.

65. Bishara J, Leibovici L, Ashkenazi S, Samra Z, Pitlik S. Seven year study of bacteremic pneumonia in a single institution. Eur J Clin Microbiol Infect Dis 2000 Dec; 19(12)926-31.

66. Lim WS, Macfarlane JT, Boswell T, et al. Study of Community-Acquired Pneumonia aetiology (SCAPA) in adults admitted to hospitals: implications for management guidelines. Thorax 2001; 56(4):296-301.

67. Carlos C. Antimicrobial Resistance Surveillance Program (ARSP) of the Department of Health (DOH), Philippines, 1999-2003.

68. Woodhead M. Prospective study of the etiology and outcome of pneumonia in the community. Lancet 1987:671-4.

69. Mundy LM, Oldah D, Auwaerten PG, et al. Implications for macrolide treatment in CAP. Chest 1998; 113(5):1201-6.

70. British Thoracic Society Guidelines for the management of CAP in Adults. Thorax 2001; 56 Suppl 4; 1-64.

71. Calver, AD, Walsh NS, Quinn PF, et al. Dosing of amoxcillin/calvulanate given every 12 hours is as effective as dosing every 8 hours for treatment of Lower Respiratory Tract Infection. Clin Infect Dis 1997 Apr 24(4):570-4.

72. Higuera F, Hidalgo H, Feris J, Giguere G, Colins J. Comparison of oral cefuroxime axetil and oral amoxicillin/ clavulanate in the treatment of Community-Acquired Pneumonia. J Antimicrob Chemother 1996; 37(3):555-64.

73. Genne D, Siegrist H, Humair L, Janin B, de Torrente A. Clarithromycin versus amoxicillin-clavulanic acid in the treatment of community-acquired pneumonia. Eur J Clin Microbiol Infect Dis. 1997;16(11):783-8.

74. Rovira E, Martinez E, Belda A, Gonzalvo F, Ripolles F, Pascual J. Treatment of Community-Acquired Pneumonia in outpatients: randomized study of clarithromycin alone versus clarithromycin and cefuroxime. Respiration 1999;66(5):413-8.

75. Grimaldo ER, Tupasi TE, Rivera AB, et al. Increased resistance to ciprofloxacin and ofloxacin in MDR-MTB isolates from patients seen at a tertiary hospital in the Philippines. Int J Tuberc Lung Dis 2001 5(6):546-50.

76. Williams JH. Fluoroquinolones for Respiratory Infections: Too valuable to Overuse. Chest 2001; 120(6):1771-5.

77. Ginsberg A, Hoper N, Parrish N, et al. Fluoroquinolone Resistance in Patients with Newly Diagnosed Tuberculosis. Clin Infect Dis 2003; 37: 1448-52.

78. Okimoto N, Kurihara T, Honda N, et al. Clinical effect of Ampicillin with beta-lactamase inhibitor (sulbactam/ampicillin) on Community-Acquired Pneumonia in the elderly. *J Infect Chemother* 2003 Jun; 9(2): 183-6.

79. Jauregui L, Minns P, Hageage G. A comparison of ampicillin/sulbactam versus cefotaxime in the therapy of lower respiratory tract infections in hospitalized patients. J Chemother. 1995; 7(2): 153-6.

80. Ortiz G. Lopez J, Friedland I, et al. A study evaluating the efficacy, safety and tolerability of ertapenem vs. ceftriaxone for the treatment of CAP in adults. Clin Infect Dis 2002; 34(8): 1076-83.

81. Vetter N, Hernandez E, Rohlf J, et al.A prospective, randomized double-blind multicenter comparison of parenteral ertapenem & ceftriaxone for the treatment of hospitalized adults with Community-Acquired Pneumonia. Clin Ther 2002; 24(11): 1770-85.

82. Frank E, Liu L, Kinasewitz G, et al. A multi-center open label, randomized comparison of levofloxacin and azithromycin plus ceftriaxone in hospitalized adults with moderate to severe Community-Acquired Pneumonia. Clin Ther 2002; 24 (8): 1292 – 308.

83. Siasoco B, Bobadilla J, Chavez J, Lazo S, Espallardo N. A Randomized Controlled Trial comparing the effectiveness and safety of once daily Levofloxacin versus ceftriaxone with or without erythromycin in the treatment of Community-Acquired Pneumonia. Phil J Int Med 2000; 38:26-31.

84. File T, Segreti J, Dunbar L, et al. A Multicenter, randomized study comparing the efficacy and safety of intravenous and/or oral Levofloxacin versus ceftriaxone and/or cefuroxime axetil in treatment of adults with CAP. Antimicrob Agents Chemother 1997; 41(9):1965-72.

85. Dresser LD. Cost-effectiveness of gatifloxacin vs ceftriaxone with a macrolide for the treatment of Community-Acquired Pneumonia. Chest 2001; 119(5):1439-48.

86. Sanchez F, Mensa J, Martinez E, et al. Is Azithromycin the 1st choice macrolide for treatment of Community-Acquired Pneumonia? Clin Infect Dis 2003; 36(10):1239-45.

87. Pena A, Roa C, Makalintal N, et al. et al. Safety and efficacy of IV and oral Azithromycin in Community-Acquired Pneumonia: results of an open, multi-center study among Filipino patients. Phil J Int Med 2003; 41:51-8.

88. Contopoulos DG, Joannidis J, Chaw P, Lau J. Meta-analysis of Randomized Controlled Trials on the comparative efficacy and safety of azithromycin against other antibiotics for Lower Respiratory Tract Infection. J Antimicrob Chemother. 2001;48(5):691-703; J Antimicrob Chemother 2002; 50(3):433-4.

89. Plouffe JF, Breiman RF, Fields BS, et al. Azithromycin in the Treatment of Legionella pneumonia requiring hospitalization. Clin Infect Dis 2003; 37 (11):1475-80

90. McCarty JM. Clarithromycin in the management of Community-Acquired Pneumonia. Clin Ther 2000 Mar 22(3):281-94; discussion 265.

91. Feagan BG. A controlled trial of a critical pathway for treating Community-Acquired Pneumonia: the CAPITAL study assessing levofloxacin. Pharmacotherapy. 2001;21(7 Pt 2):89-94S.

92. Hurst M, Lamb H, Scott L, Figgitt D. Levofloxacin: an updated review of its use in the treatment of bacterial infections. Drugs 2002; 62(14):2127-67.

93. Dunbar L, Wunderink R, Habib M, et al. High-Dose, Short Course Levofloxacin for Community-Acquired Pneumonia: A New Treatment Paradigm. Clin Infect Dis 2003:37:752-60.

94. Erard V, Lamy O, Bochud PY, Bille J, Cometta A, Calandra T. Full course oral levofloxacin for treatment of hospitalized patients with Community-Acquired Pneumonia. Eur J Clin Microbiol Infect Dis 2004; 23(2):82-8.

95. Lin JC, Yeh KM, Peng MY, Chang FY. Efficacy of cefepime versus ceftazidime in the treatment of adult pneumonia. J Microbiol Immunol Infect. 2001; 34(2):131-7.

96. Shlaes DM, Baughman R, Boylen CT, et al. Piperacillin/tazobactam compared with Ticarcillin/clavulanate in community-acquired bacterial lower respiratory tract infection. J Antimicrob Chemother 1994 ;34(4):565-77.

97. Speich R, Imhof E, Vogt M, Grossenbacher M, Zimmerli W. Efficacy, safety and tolerance of Piperacillin/tazobactam compared to Co-amoxiclav plus an Aminoglycoside in the treatment of severe pneumonia. Eur J Clin Microbiol Infect Dis 1998; 17(5):313-7.

98. Finch RG, Pemberton K, Gildon KM. Pneumonia: the impact of risk factors on the outcome of treatment with meropenem and ceftazidime. J Chemother 1998;1:35-46.

99. Romanelli G. Cravarreza P, Pozzi A, et al. Carbapenems in the treatment of severe Community-Acquired Pneumonia in hospitalized elderly patients: a comparative study against standard therapy. J Chemother 2002; 14(6):609-17.

100. Ho A, Leung R, Lai CK, Chan TH, Chan CH. Hospitalized Patients with Community-Acquired Pneumonia in Hong Kong: a randomized study comparing imipenem/cilastin and ceftazidime. Respiration 1997;64(3): 224-8; 64(4):303.

101. Bartoloni A, Strohmeyer M, Corti G, et al. Multicenter randomized trial comparing meropenem and imipenem/cilastin in the hospital treatment of Community-Acquired Pneumonia. Drugs Exp Clin Res. 1999;25(6):243-52.

102. Beaucaire G , Leroy O, Beuscart C, Karp P, Chidiac C, Caillaux M. Clinical and bacteriological efficacy and practical aspects of amikacin given once daily for severe infections. J Antimicrob Chemother 1991; 27 Suppl C: 91-103.

103. Covi M, Velluti G. Comparison of the efficacy and safety of isepamicin and amikacin the treatment of acute lower respiratory tract infections caused by Gram-negative organisms. J Chemother 1995; 7 Suppl 2:137-42.

104. Pachon, J, Prados MD, Capote F, Cuello JA, Garnacho J, Verano A. Severe Community-Acquired Pneumonia: Etiology, prognosis, and treatment. Am Rev Respir Dis 1990; 142: 369-73.

105. Halm E, Fine M, Marrie T, et al. Time to Clinical Stability in patients hospitalized w/ Community-Acquired Pneumonia: Implications for Practice Guidelines. JAMA 1998; 279(18); 1452-57.

106. Dans PE, Charache P, Fahey M, Otter SE. Management of Pneumonia in the prospective payment era: a need for more clinician and support service intereaction. Arch. Intern Med 1984; 144:1392-7.

107. Marrie TJ, Durant J, Yates L. Community-acquired Pneumonia requiring hospitalization: 5 year prospective study. Rev Infect Dis 1989;11(4):586-99.

108. Mittl, RL, Schwab RI, Duchin JS, Goih JB, Albeida SM, Miller W. Radiographic resolution of Community-Acquired Pneumonia. Am J Respir Crit Care Med 1994; 149: 630-5.

109. Jay S, Waldemar J, Pierce A. The Radiologic resolution of S. pneumoniae pneumonia. N Engl J Med 1975; 293: 798-801.

110. Macfarlane, JT, Miller AC, Roderick Smith WH, Morris AH, Rose DH. Comparative radiographic features of community-acquired legionnaires' disease, pneumococcal pneumonia, M. pneumoniae and Psitacosis. Thorax 1984; 39: 28-33.

111. El Solh A, Aquilina A, Gunen H, Ramadan F. Radiographic resolution of community-acquired bacterial pneumonia in the elderly. J Am Geriatr Soc 2004;52(2):224-9

112. Grayston JT. Chlamydia pneumoniae, strain TWAR pneumonia. Ann Rev Med 1992; 43: 317-23.

113. Hitt CM, Nightingale CH, Quintiliani R, Nicolau DP. Streamlining antimicrobial therapy for lower respiratory tract infections Clin Infect Dis 1997; 24(Suppl 2):S213-7.

114. Vogel, F. IV/oral sequential therapy in patients hospitalized w CAP. W/c patients, when & what agents? Drugs 2002: 62(2):309-17.

115. Ramirez JA, Vargas S, Ritter G, et al. Early switch from IV to oral antibiotics and early hospital discharge: a prospective observation study of 200 consecutive patients with Community Acquired Pneumonia. Arch Intern Med 1999; 159: 2449-54.

116. Milkovich G. IV to oral transition therapy in Community-Acquired Pneumonia: The INOVA Health System Experience. Pharmacotherapy 2001 21(7s): 83-88.

117. Ramirez, JA. Managing Antiinfective Therapy of Community-Acquired Pneumonia in the Hospital setting: Focus on switch therapy. Pharmacotherapy 2001 21(7s):79-82

118. Ramirez, JA, Bordon J. Early Switch from Intravenous to Oral Antibiotics in Hospitalized Patients With bacteremic Community-Acquired *Streptococcus pneumoniae* Pneumonia. Arch Intern Med 2001; 161(6):848-50.

119. Finch R, Schurmann D, Collins O, et al. Randomized Controlled Trial of Sequential I.V. and Oral Moxifloxacin Compared with Sequential I.V. and Oral Co-amoxiclav with or without Clarithromycin in patients with CAP requiring initial parenteral treatment. Antimicrob Agents Chemother 2002; 46(6):1746-54.

120. Lode H, Grossman C, Choudhri S, et al. Sequential IV/PO moxifloxacin treatment of patients with severe Community-Acquired Pneumonia. Respir Med 2003; 97(10):1134-42.

121. Halm EA, Switzer G, Mittman B, Walsh M, Chang C, Fine M. What factors influence physicians' decisions to switch from IV to oral antibiotics for Community-Acquired Pneumonia? J Gen Intern Med 2001:16:599-605.

122. Cockburn J, Gibberd RW, Reid AL, Sanson RW. Determinants of non-compliance with short-term antibiotic regimens. Br Med J 1987; 295: 814-18.

123. Finch RG, Woodhead MA. Practical Considerations and Guidelines for the Management of Community-Acquired Pneumonia. Drugs. 1998;55(1):31-45.

124. Siegel R, Halpern N, Almenoff P, Lee A, Cashin R, Greene J. A prospective randomized study of inpatient IV antibiotics for Community-Acquired Pneumonia: The Optimal Duration of Therapy Chest 1996; 110(4): 965-71.

125. Siegel R, Alicea M, Lee A, Blaiklock R. Community-Acquired Pneumonia: Determination of the Optimal Duration of Therapy. Chest 1997; 112(3) Suppl 3 5S-6S.

126. Siegel RE, Alicea M, Lee A, Blaiklock R. Comparison of 7 versus 10 days of antibiotic therapy for hospitalized patients with uncomplicated Community-Acquired Pneumonia: a prospective, randomized, double blind study. Am J Ther 1999;6(4):217-22.

127. Myburgh J, Nagel GL, Perschel E . The efficacy and tolerance of a 3 day course of azithromycin in the treatment of Community-Acquired Pneumonia. J Antimicrob Chemother 1993;31(Suppl E):163-70.

128. Zachariah J. A randomized, comparative study to evaluate the efficacy and tolerability of a 3 day course of azithromycin versus a 10 day course of co-amoxiclav as tx for adult patients with lower respiratory tract infections. J Antimicrob Chemother 1996; 37 Suppl C; 103-13.

129. Rizzato G, Montemurro L, Fraioli P, et al. Efficacy of a 3 day course of azithromycin in moderately severe community-acquired pneumonia. Eur Respir J 1995; 8(3): 398-402

130. O'Doherty B, Muller O. Randomized, Multicenter Study of the Efficacy and Tolerance of Azithromycin versus Clarithromycin in the treatment of Adults with mild to Moderate CAP. Eur J Clin Microbiol Infect Dis 1998 17:828-33.

131. Mandell L, File T. Short-Course Treatment of Community-Acquired Pneumonia. Clin Infect Dis 2003:37:761-3.

132. CDC. Prevention of Pneumococcal Disease: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 1997;47(No.RR-8).

133. CDC.Prevention and Control of Influenza: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2004.

134. Philippine Society for Microbiology and Infectious Diseases and Philippine Foundation of Vaccination. Routine Adult Immunization for Filipinos. 2003

135. Council on Lung Infections, Philippine College of Chest Physicians. Recommendations for Adult Vaccination Against Lung Infections. 2003

136. DOH Technical Working Group for Influenza Prevention & Management. Guidelines on Prevention and Management of Influenza. DOH Administrative Order No. s. 2003

137. Capeding MRZ, Sombrero LT, Lucero MG, Saniel MC. Serotype distribution and antimicrobial resistance of invasive *Streptococcus pneumoniae* isolates in Filipino children. Jour Infect Dis 1994; 169:479-480.

138. Gross PA, Hermogenes AW, Sacks H, Lau J, Levandowski R. The Efficacy of influenza vaccine in elderly persons: a meta-analysis and review of literature. Ann Intern Med 1995;123 (7):518-27.

139. Mullooly JP, Bennett MD, Hombrook MC, et al. Influenza vaccination programs for elderly persons: cost-effectiveness in a health maintainance organization. Ann Intern Med 1994;121:947-52

140. WHO. Amid SARS concerns, WHO urges influenza vaccinations for high-risk groups. 2 September 2003.

141. Chan V. Epidemiological Data on Influenza in the Philippines. First International Symposium on Adult Immunization in Asia: Prevention of Influenza and Pneumococcal Infections. Hanoi, Socialist Republic of Vietnam 1998 April 20, 22; 35-7.

142. Govaert TM, Thijs CT, Masurel N, Sprenger MJ, Dinant GJ, Knottnerus JA. Efficacy of influenza vaccination in elderly individuals: a randomized double-blind placebo-controlled trial. JAMA 1994;272:1661-5

143. Margolis KL, Nichol KL, Poland GA, Pluhar RF. Frequency of adverse reactions to influenza vaccine in the elderly: a randomized controlled trial. JAMA 1990;264:1139-41

144. Butler JC, Shapiro ED, Carlone GM. Pneumococcal vaccines: History, current status and future directions. Am J Med. 1999; 107 (1A): 69S-76S.

145. Shapiro ED, Berg AT, Austrian R, et al. The protective efficacy of polyvalent pneumococcal polysaccharide vaccine. NEJM 1991; 325:1453-1460.

146. Forrester BL, Jahnigan DW, LaForce FM. Inefficacy of pneumococcal vaccine in a high risk population. Am J Med. 1987;83:425-430.

147. Jackson LA, Neuzil KM, Yu O, et al. Effectiveness of pneumococcal polysaccharide vaccine in older adults. NEJM 2003; 348(18): 1747-1755.

148. Wilde JA, Mcmillan JA, Serwint J, Butta J, O'Riordan MA, Steinhoff MC.. Effectiveness of vaccination against influenza in health care professionals. JAMA 1999;281(10):908-13.

149. Bridges CB, Thompson WW, Meltzer MI, et al. Effectiveness and cost benefit of influenza vaccination in healthy working adults: a randomized controlled trial. JAMA 2000;284:1655-63.

150.Ahmed F, Singleton JA, Franks AL. Influenza vaccination for healthy young adults. NEJM 2001; 345:1543-1547.

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

   Level of Quality of Evidence for Treatment Trials:

Level	Criteria
I	Evidence from at least one properly randomized controlled trial (Criteria a and b are satisfied)

II 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)

III Evidence from opinions of respected authorities on the basis of clinical experience, descriptive studies, or report of expert committees.

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 consecutives 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:

I a + b + c + d
II a + b + e + d
III Retrospective study
IV Patients were non-consecutive, selected because of definitive results of the finding under study.
V Unclear gold standard or poorly defined population.

3. *Studies on prognosis or causation*

Criteria for assessing quality of evidence

A. An inception cohort was chosen
B. Reproducible inclusion and exclusion criteria sere used

C. Follow-up was complete for at least 80% of subject
D. Statistical adjustment was carried out for confounders or extraneous factors
E. Reproducible descriptions of outcome measures were used

Level of Quality of Evidence

I. All of the following criteria must be satisfied.
II. An inception cohort was selected but only 3 or 4 remaining criteria were satisfied.
III. An inception cohort was selected but only 2 or 4 remaining criteria were satisfied.
IV. An inception cohort was selected but only 1 or 4 remaining criteria were satisfied.
V. An inception cohort was selected but only 1 or 4 remaining criteria were satisfied.
VI. None of the 5 criteria was met.

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
I. All 4 of the following criteria must be met.
II. 3 of the 4 criteria are met.
III 1 of the 4 criteria is met.
IV. 1 of the 4 criteria is met.
V. None of the 4 criteria are met.

ACKNOWLEDGMENT

We gratefully acknowledge the participation of the following members of the 1998 Task Force on CAP for their invaluable contribution to the development of the initial CAP Guideline.

Felicita S. Medalla, MD
Ismael G. Sumagaysay, MD
Ma. Imelda Quelapio, MD
Cecille A. Taguinod, MD

We appreciate the efforts of *Dr. Marissa M. Alejandria* and *Dr. Regina P. Berba* for the critical appraisal of references.

We also thank the participants of the public forum representing the different institutions and organizations listed hereafter, whose significant comments and suggestions were considered in the final draft.

Public Forum Participants

Organizations

Philippine Medical Association	*Atty. Leo O. Olarte, MD*
Philippine Society for Microbiology & Infectious Diseases	*Evelina N. Lagamayo, MD*
	May B. Montellano, MD
	Jaime C. Montoya, MD
	Lita C. Vizconde, MD
	Ludovico L. Jurao, Jr., MD
Philippine College of Physicians	*Adrian C. Peña, MD*
Philippine College of Chest Physicians	*Merci Gappi, MD*
	Rene Juaneza, MD
	Mario Juco, MD
	Sylvia Yang, MD
	JenniferAnn Mendoza-Wi,MD
	Tiburcio Leonin, MD
	Parkash Mansukhani, MD
	Ivan Villespin, MD
American College of Chest Physicians (Philippine Chapter)	*Isaias A. Lanzona, MD*
Philippine Academy of Family Physicians	*Arlette Samaniego, MD*
	Leilanie Apostol-Nicodemus, MD
	Ma. Cecilia Cuaresma-Cruz, MD
	Ronaldo E. Lapitan, MD
Philippine Academy of Medical Specialists	*Miguel T. Ocampo, MD*
Philippine Nurses Association	*Leah Primitiva Samaco-Paguiz, MD*

Institutions

Department of Health	*Jaime Y. Lagahid, MD*
	Lyndon L. Lee Suy, MD
UP-Philippine General Hospital	*Regina P. Berba, MD*
	Mario R. Festin, MD
Research Institute for Tropical Medicine	*Rossana A. Ditangco, MD*
	Josephine O. Marcos, MD
	Menette Panaligan, MD
Santo Tomas University Hospital	*Remedios F. Coronel, MD*
University of the East –RMMMC	*Vicente Jr., Tanseco, MD*
Lung Center of the Philippines	*Juanito A. Rubio, MD*
Philippine Heart Center	*Teresita De Guia, MD*
Makati Medical Center	*Raul G. Fores, MD*
San Lazaro Hospital	*Arturo B. Cabanban, MD, MHA*
Manila Doctors Hospital	*Ma. Cecilia S. Montalban, MD*
Armed Forces of the Phil. Medical Center	*Alberto I. Gabriel, MD*
Veterans Memorial Medical Center	*Victoria Icasiano-Javier, MD*
St. Luke's Medical Center	*Dionisio M. Tiu, MD*
Perpetual Help Medical Center	*Jose Edzel V. Tammo, MD*
Davao Doctors Hospital	*Crisostomo Serrano, MD*

Pharmaceuticals

Abbott Laboratories	*Bienvenido V. Tiangco, MD*
Aventis Pasteur	*Ruby Dizon, MD*
Bristol-Myers Squibb	*Jaime Montoya, MD*
GlaxoSmithKline	*Carla Avis*
Bayer Philippines, Inc.	*Leandro Bongosia, MD*
Merck Sharp & Dohme	*Cesar S. Recto II, MD*
	Cecille Montero
Pascual Laboratories, Inc.	*Kurt Glenn Jacoba, MD*
Pfizer Philippines, Inc.	*Cristobal C. Dumo, MD*
Roche Philippines, Inc.	*Nicanor Pallingayan*
Wyeth Philippines, Inc.	*Nerissa C. Calimon, MD*
Zuellig Pharma Corporation	*Santiago V. Guzman, MD*

Secretariat

Iris K. Maranan
Rosa Lydia L. de Guzman

Philippine Practice Guidelines Group - Infectious Diseases
Philippine Society for Microbiology and Infectious Diseases
No. 116 9th Avenue, Cubao
Quezon City 1109 Philippines

ISBN # 971-92130-4-3