International CAPO Study Protocol

"An International, Observational Study to Evaluate Current Management of Hospitalized Patients with Community-Acquired Pneumonia"

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(For a complete list of participating sites, please see Appendix A)

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1. Background & Rationale

Community-acquired pneumonia (CAP) is a very common infection and remains a very common cause of mortality worldwide. In an attempt to improve patient outcome, national organizations from several countries have developed guidelines for the management of patients with CAP. The first US national guidelines were published by the American Thoracic Society (ATS) in 1993.[1] Since then, several other national organizations in the US have recommended guidelines for management of patients with CAP, as well as quality indicators to evaluate the actual management of patients with CAP. They include the Infectious Diseases Society of America (IDSA),[2] the Centers for Disease Control and Prevention (CDC),[3] the Joint Commission on Accreditation of Healthcare Organizations (JCAHO),[4] and the Department of Health and Human Services Health Care Financing Administration (HCFA).[5] The primary premise during the creation of a guideline document is that dissemination of the guidelines will alter care at the local level and, with time, the current management of patients with CAP will be in compliance with the management recommended by national guidelines. Although a tremendous amount of resources are being expended in the development and dissemination of national guidelines, there is little evidence that the plethora of recommendations has significantly closed the gap between the local current management and the management recommended by the national guidelines.

One basic problem in the evaluation of the effect of national guidelines on local practice is the paucity of data regarding the current management of hospitalized patients with CAP, and how closely the current management follows the national recommendations. Most of the published literature in the management of patients with CAP is based on

prospective therapeutic clinical trials. In these trials, patients are managed according to a predetermined clinical protocol that usually involved extensive clinical and laboratory evaluations. Since the management of patients enrolled in clinical trials is usually beyond the local standard of care, data from clinical trials cannot be used as representative of every day local practice. It should be recognized that management of a patient outside of a recommended guidelines does not necessarily indicate poor patient care. If variance exists, it is necessary to know if the variance should be considered clinically justified or unjustified. Identification of unjustified variance is important to develop and implement specific educational programs or other necessary tools aimed to move local physician practice closer to the practice recommended by national guidelines.

2. Objectives

The primary objective of this study is to define the current management of hospitalized patients with CAP with the goal to define the proportion of patients who are managed in compliance with the care recommended by national organizations. Secondary objectives of this study are to identify the reasons for variance from recommended care, and to establish what percentage of variance from recommended care should be considered clinically justified.

3. General Description of the Study

Since the goal of this study is to evaluate actual practice, the data on practice will be collected from the medical record with a retrospective review of the case after hospital discharge. All medical records that hold a diagnosis of CAP according to admitting physician will be considered eligible for review. Since this is a retrospective, observational study, there will be no clinical or laboratory procedure required by protocol. Each patient will be identified by the initials of first, middle, and last name, and will be given a code number. Data on a series of quality indicators will be collected to define the actual management of hospitalized patients with CAP, and to evaluate if variance from recommended care was present. If variance is identified, the case will be analyzed by one of the institution's investigators in an attempt to define the reason for deviation from recommended care. Based on this analysis, the variance will be defined as clinically justified or unjustified. Quality indicators used in this study were devised by the principal investigators based on a review of the literature and considering the management of CAP proposed by the ATS [1] and IDSA.[2] Not all quality indicators will be applicable to all participating hospitals. For each particular indicator, the option of not applicable will be an acceptable answer. The duration of the study will be approximately 12 months. It is expected that the management of at least 5,000 hospitalized patients with CAP will be evaluated.

4. Areas of Practice and Quality Indicators for CAP

The management of CAP will be evaluated in 7 areas of practice. For each area of practice, data on a series of quality indicators will be collected to evaluate current management. Since it is expected that some quality indicators will not apply in some institutions, the option not applicable will be available for each indicator.

4.1 Area of practice 1: Diagnosis of CAP. Inclusion criteria for making a correct diagnosis of CAP will be met if the patient presented with a new pulmonary infiltrate associated with at least one of the following: fever or hypothermia; changes in WBC (leukocytosis or leukopenia by lab); or supporting signs and symptoms (new/increased cough, new/increased sputum, or rales, wheezes or rhonci). [1,2] The subject will be excluded from the study if it was transferred directly after already being hospitalized for 48 hours or more and the information from the previous hospitalization is not available, or if it is diagnosed with hospital acquired pneumonia.

Pneumonia will be considered community-acquired if patients had no history of hospitalization during the 2 weeks prior to admission. To increase adherence to guidelines, several institutions have developed a preprinted form with a series of orders that apply to all hospitalized patients with CAP. The use of the local preprinted order form as soon as the clinical diagnosis of CAP was performed will be evaluated. **Quality indicator 1A:** Proportion of patients that met inclusion and exclusion criteria for diagnosis of CAP. **Denominator:** The total number of hospitalized patients with a diagnosis of CAP according to admitting physician.

4.2 Area of practice 2: Characteristics at hospital admission. The patients severity of illness at the time of admission will be evaluated according to the patients risk class [6] and

other severity scores. Several clinical and laboratory characteristics putting the patients at risk for a complicated course will also be evaluated.[1] Hospitalization will be considered appropriate if patients: a) were stratified to a risk class III, IV, or V, or b) had more than one risk factor for a complicated course. **Quality indicator 2A:** Proportion of patients hospitalized with risk class III to V. Denominator: The total number of hospitalized patients who met inclusion and exclusion criteria for diagnosis of CAP. **Quality indicator 2B:** Proportion of patients hospitalized with >1 risk factor criteria for a complicated course. Denominator: The total number of hospitalized patients who met inclusion and exclusion criteria for diagnosis of CAP.

4.3 Area of practice 3: Microbiological work-up. Microbiological work-up for CAP will consist of: a) sputum Gram stain and culture, b) blood cultures, c) Legionella urinary antigen, d) Streptococcus urinary antigen, and e) flu test (during flu season). **Quality indicator 3A:** Proportion of patients with sputum Gram stain and culture obtained. Denominator: The total number of hospitalized patients who met inclusion and exclusion criteria for diagnosis of CAP. **Quality indicator 3B:** Proportion of patients with blood culture obtained. Denominator: The total number of hospitalized patients who met inclusion and exclusion criteria for diagnosis of CAP. **Quality indicator 3C:** Proportion of patients with Legionella urinary antigen obtained. Denominator: The total number of hospitalized patients who met inclusion and exclusion criteria for diagnosis of CAP. **Quality indicator 3D:** Proportion of patients with Streptococcus urinary antigen obtained. Denominator: The total number of hospitalized patients who met inclusion and exclusion criteria for diagnosis of CAP. **Quality indicator 3E:** Proportion of patients with flu test obtained. Denominator: The total number of hospitalized patients who met

inclusion and exclusion criteria for diagnosis of CAP.

4.4 Area of practice 4: Empiric therapy. Criteria for optimal antibiotic therapy will be met when: a) the antibiotic selection (drug) was in compliance with suggested therapy, [1,2] **Quality indicator 4A:** Proportion of patients with antibiotic selection compliant with guideline. Denominator: The total number of hospitalized patients who met inclusion and exclusion criteria for diagnosis of CAP.

4.5 Area of practice 5: Clinical course. A patient will be considered a candidate for switch from intravenous to oral antibiotics when the following four criteria are met during the first week of hospitalization: 1) cough and shortness of air were improving, 2) patient was afebrile for at least 8 hours, 3) the white blood cell count was normalizing, and 4) oral intake and gastrointestinal absorption were adequate.[8] Criteria for switch therapy will be met when: a) the switch to oral therapy was carried out no more than 24 hours after the patient became a switch therapy candidate, and b) the selection of the oral antibiotic was compliant with guidelines. **Quality indicator 5A:** Proportion of patients in whom switch therapy was performed. Denominator: The total number of hospitalized CAP patients who became switch therapy candidates during the first seven days of hospitalization. **Quality indicator 5B:** A Proportion of patients switched to appropriate oral antibiotics. Denominator: The total number of hospitalized CAP patients who were switched to oral antibiotics.

4.6 Area of practice 6: Evaluation of clinical outcome. Criteria will be met when clinical outcome was adequately documented. The clinical outcome will be classified as early outcome and final outcome. Evaluation of the patient at hospital discharge will be defined as early outcome. Evaluation of the patient 30 days will be defined as final

outcome. **Quality indicator 6A:** Proportion of patients with known final clinical outcome. Denominator: The total number of hospitalized patients who met inclusion and exclusion criteria for diagnosis of CAP.

4.7 Area of practice 7: Prevention of pneumonia. Criteria for appropriate prevention of pneumonia will be met when: a) patients were either given the polyvalent pneumococcal polysaccharide vaccine or evaluated for the need to receive the vaccine, b) patients were either given influenza vaccine or evaluated for the need to receive the vaccine, and c) smoking cessation was offered. **Quality indicator 7A:** Proportion of patients evaluated for, or given pneumococcal vaccine. Denominator: The total number of discharged patients who met inclusion and exclusion criteria for diagnosis of CAP. **Quality indicator 7B:** Proportion of patients evaluated for, or given flu vaccine. Denominator: The total number of discharged patients during the influenza season who met inclusion and exclusion criteria for diagnosis of CAP. **Quality indicator 7C:** Proportion of patients who had smoking cessation offered. Denominator: The total number of discharged patients who met inclusion and exclusion criteria for diagnosis of CAP and were active smokers.

5. Study Criteria

Inclusion Criteria

1. Age 18 years and older.
2. Community-acquired pneumonia, defined as follows:

   A. Chest imaging with evidence of new pulmonary infiltrate obtained within 48 hours before or 48 hours after time of arrival.

   B. One of these:

   □ Fever ≥ 38°c/100.4°f or hypothermia ≤ 35.5°c/95.9°f.

   □ Changes in wbc (leukocytosis or leukopenia by lab)

   □ Supporting signs and symptoms:

   □ New/increased cough □ New/increased sputum □ Rales, wheezes or rhonci

Exclusion Criteria

1. Transferred directly after already being hospitalized for 48 hours or more and the information from the previous hospitalization is not available.
2. Hospital acquired pneumonia.

6. Data Collection

Data on patient demographics, baseline characteristics, course of the disease, antimicrobial use, clinical management, laboratory and radiographic tests will be transferred from the medical record to a data collection form. Data will be de-identified by assigning a code to each patient. Each study center will be given a data collection manual with clear rules for data entry.

7. Data Management

Each study site will be given a data base management software. Data will be entered in a local computer and transferred to a central database at the Division of Infectious Diseases, University of Louisville. Data will be evaluated for consistency among variables. Missing, out-of-range, or illogical data will generate corrective actions. Descriptive statistics will be performed at periodic intervals during the study to evaluate for unexpected distributions. Data will be analyzed by descriptive and analytic statistics at the end of study period.

8. Institutional Review

This research is a retrospective review of the subjects' medical records and involves no more than minimal risk to the subjects. The Institutional Review Board (IRB) will approve the protocol for this study. All changes to the protocol, as well as a change of principal investigator, will also be approved by the IRB. Records of the IRB review and approval of all documents pertaining to the study will be kept on file by the investigator. IRB approval will be obtained each year of study.

9. References

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8. Ramirez JA, Vargas S, Ritter GW, Brier ME, Wright A, Smith S, Newman D, Burke J, Mushtaq M, Huang A. Early switch from intravenous to oral antibiotics and early hospital discharge. A prospective observational study of 200 consecutive patients with community-acquired pneumonia. Arch Intern Med. 1999; 159:2449-2454.

Appendix A: Participating Sites

University of Louisville, Louisville, Kentucky USA ; VA Medical Center, Louisville, Kentucky; USA S Maria delle Misericordia, Udine, Italy; Hospital de Clinicas, Jose de San Martin, Buenos Aires, BA Argentina; Johannesburg Hospital, Johannesburg, Gauteng, South Africa; Hosiptal Universitario de Caracas, Caracas, Distrito Metropolitano, Venezuela; Clinica San Pabla, Lima, Lima Peru ; Instituto de Neumonologia y Cirugia Toracica, Barcelona, Spain; Instituto Nacional del Torax, Santiago, Chile; Hackensack University Medical Center, Hackensack, NJ USA; Pico, Milan, Italy; Ospedale L. Sacco, Milan, Italy ; Hospital Dr. Oscar Allende, Mar del Plata, BsAs, Argentina; University of Alberta Hospital, Edmonton, Alberta, Canada; Hospital Clinico Regional, Valdivia, Chile; University of Santo Tomas Hospital, Manila, Philippines ; Instituto Medico Plantense, La Plata, BsAs, Argentina ; Hospital Universitario Joan XXIII de Tarragona, Tarragona, Spain ; Hospital Maisonneuve-Rosemont, Montreal QC, Canada; National Kidney and Transplant Institute, Quezon City, Metro Manila, Philippines; QE II Health Sciences Centre, Halifax, NS, Canada ; University Medical Center, GA, Utrecht, The Netherlands; University of Michigan Health System, Ann Arbor, MI USA ; Hospital de Clinicas de Porto Alegre, Porto Alegre, RS, Brazil ; IRCCS Fondazione Policlinico, Milan, Italy; Mackay Memorial Hospital, Taipei, Taiwan, Republic Of China ; City Hospital E.v.Behring/Lungenklinik Heckeshom, Berlin, Germany; C van Buren, Valparaiso, Quinta Region, Chile ; Henderson Hosital, Hamilton, Ontario, Canada; IDIMA Lanari, Buenos Aires, Argentina ; Hospital Luis Gomez Lopez-Ascardo, Barquisimeto, Lara, Venezuela; Hospital Nacional Roosevelt, Guatemala ; Hospital Sant Pau i Santa Teele, Tarragona, Spain ; Northeastern Ohio Universities, Akron, Ohio USA ; Apollo Hospital, Chennai, TN, India ; LDS Hospital Salt Lake City, Utah, USA ; Hospital Miguel Perez Carreno, Caracas, D.D. Venezuela ; Hospital Nostra Senyora de Meritxell Escaldes, Engordany, Andorra, Andorra ; All India Institute of Medical Sciences, New Delhi, India ; Toronto General Hospital, Toronto Western Hospital, Toronto, Ontario, Canada; LDS Hospital, Salt Lake City, Utah, USA; Royal Alexandre Hospital, Edmonton, Alberta, Canada ; Misericordia Hospital, Edmonton, AB, Canada ; Grey Nuns Hospital, Edmonton, AB, Canada; Hospital Univrsitario La Fe, Valencia, Valencia, Spain ; University of Texas Health Science Center, San Antonio, Texas, USA; Ponificia Univesidad Catolica de Chile, Santiago, Santiago, Chile ; Hospital Enrique Tomu, Buenos Aires, BsAs, Argentina; Hospital Universitario Austral, Pilar, Buenos Aires, Argentina ; Hospital Francisco J. Muniz, Buenos Aires, Buenos Aires, Argentina; Sanatorio 9 de Julio, San Miguel de Tucuman, Tucuman, Argentina ; Clinica Uruguay, Concepcion del Uruguay, Entre Rios, Argentina; Centro de Tratamiento Intensivo-Hospital Maciel, Montevideo, Montevideo, Uruguay; Corporacio Sanitaria Parc Tauli, Sadabell, Barcelona, Spain; Providence Hospital, Washington, DC USA; Southern Arizona VA Healthcare System Hospital, Tucson, Arizona USA; Hospital de Pulido Valente, Lisboe, Lisboe, Portugal ;

University Hospital, San Antonio, Texas USA; Hospital Pasteur, Montevideo, Montevideo, Uruguay ; Profesor Bernardo Houssay, Vicente Lopez, Buenos Aires, Argentina ; Sotina Hospital Athens, Athens, Greece ; School of Public Health and Information Sciences, Louisville, KY USA; Hospital Nacional Cayetano Heredia, Lima, Lima, Peru ; Hospital Maciel, Montevideo, Montevideo, Uruguay ; Hospital Universitario de Los Andes, Merida, Merida, Venezuela; Hospital Espanol Mendoza, Godoy Cruz, Mendoza, Argentina ; Sanatorio Otamendi Miroli, Capital Federal, Buenos Aires, Argentina ; Complejo Hospitalario Dr. Amulfo Arias Madrid, Panama, Panama ; Hospital IVSS Dr. Domingo Guzman Lander, Barcelona, Anzoategui, Venezuela; Hospital Central Dr. Urquinaona, Maracaibo, Zulia, Venezuela; Hospital Central Univ. Antonio M. Pineda, Barquisimeto, Lara, Venezuela; Hospital Militar Dr. Manuel Siverio Castillo, Guayana, Puero Wrdaz, Venezuela; Miami Valley Hosiptal, Dayton, Ohio USA ; Greene Memorial Hospital, Xenia, Ohio USA; Emory Crawford Long Hospital, Atlanta, Georgia USA; Hospital Nacional Cayetano Heredia, Lima, Peru ; Ninewells Hospital Dundee, Tayside, Scotland ; Royal Infirmary of Edinburgh, Edinburgh, Lothian, Scotland; Western General Hospital, Edinburgh, Lothian, Scotland; Hospital Pulido Valente Lisbon, Lisbon, Portugal; Norton Downtown Hospital, Louisville, Kentucky USA ; Norton Audubon Hospital, Louisville, Kentucky USA ; Norton Women's and Children's Hospital, Louisville, Kentucky USA ; Norton Brownsboro Hospital, Louisville, Kentucky USA ; Baptist East Hospital, Louisville, Kentucky USA ; Jewish Hospital, Louisville, Kentucky USA ; Sts. Mary and Elizabeth Hospital, Louisville, Kentucky USA ; Hospital de Los Angeles, Los Angeles, Bio Bio Region, Chile.