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Human Subject Study Description

Title: Pediatric-Specific Quality Measures for Community-Acquired Pneumonia

A. Study Purpose and Rationale:

Community-acquired pneumonia (CAP) remains a significant cause of childhood morbidity and mortality worldwide. It is estimated that more than 150 million cases of pneumonia occur globally each year in children under the age of five.[1] The annual incidence of pneumonia peaks within in this age group and declines steadily throughout adolescence and into early adulthood.[2-5] Pneumonia is one of the leading causes of death for children in the developing world.[6]

Despite the common nature of the condition, management of community-acquired pneumonia in children remains controversial. The Infectious Diseases Society of America (IDSA) and the American Thoracic Society (ATS) have published guidelines for the management of CAP in adults,[7-10] but no guideline has been widely accepted for pediatric patients. Groups such as the Joint Commission and the National Quality Forum (NQF) have placed an emphasis on developing standardized performance measures to assess the quality of health care. Pneumonia is one diagnosis for which these groups have chosen to study quality of care for adult patients. A number of core hospital performance measures have been suggested as indicators of quality for the care of CAP in adults. These indicators include oxygenation assessment, timing of antibiotic administration, antibiotic choice, collection of blood culture prior to antibiotic administration, and influenza and pneumococcal screening and vaccination. Each of these processes is an NQF-endorsed performance measure, Joint Commission core measure, and/or a Centers for Medicaid & Medicare Services (CMS) Hospital Quality Initiative measure;[11-14] failure to adhere to these evidence-based processes may compromise the quality of care delivered. However, the common etiologies of CAP and physiologic responses to infection are different in children as compared with adults, so these performance measures may not be appropriate for pediatric patients. Analogous national performance measures specific for pediatrics have not been developed.

In the absence of nationally accepted performance measures for pediatric CAP, there is no clear way to measure the quality of care delivered to those children diagnosed with pneumonia. One retrospective cohort study of children 18 months-18 years admitted to Children's Hospital Boston in 2003-04 assessed compliance with and applicability of adult national quality indicators in pediatric CAP.[15] The primary outcome was adherence to process measures recommended for adult CAP with additional outcomes including time to clinical stability and length of stay. Associations between adherence to individual quality measures and both time to clinical stability and length of stay were assessed. The study illustrated that quality of care indicators recommended for adults were not achieved in many pediatric patients with CAP, and that only time to antibiotic administration is predictive of more rapid stabilization or reduced length of stay. The authors proposed several quality measures more tailored to the pediatric patient population. These measures are largely similar to those employed in adult medicine but have variations based on the prevalence of respiratory failure in the pediatric population and CDC vaccination recommendations. For the purposes of this study, clinical stability is defined as resolution of fever (temperature < 38 degrees Celsius), age-appropriate respiratory rate, oxygen saturation ≥ 93% on room air, and able to take oral fluids

Table 1. Proposed Pediatric-Specific Quality Measures for CAP

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| 1. Oxygenation assessment within 4 hours of hospital arrival |
| 2. Blood culture obtained prior to antibiotic administration |
| 3. Antibiotic selection consistent with current guidelines* |
| 4. Antibiotic administration within 4 hours of hospital arrival |
| 5. Influenza screening and/or vaccination for eligible children |
| 6. Transition from intravenous to oral antibiotics upon reaching clinical stability |

* No specific guideline can be strongly recommended over any other based on evidence, but the McIntosh recommendations[16] are suggested as a reasonable guideline.

Although there is evidence suggesting improved clinical outcomes in pediatric CAP managed by clinical pathways, consensus does not exist as to whether the use of quality measures actually results in improved outcomes or higher quality of care. A recent study of adult CAP care showed that hospitals engaged in a "pay for performance" program achieved significantly greater improvements in adherence to quality indicators, including several related to CAP management, than hospitals not participating in the program.[17] This study seeks to determine if education on and basic implementation of proposed pediatric-specific quality measures for CAP result in improved inpatient outcomes.

B. Methods

Study Design:

This research will be constructed as a controlled "before and after" study.[18] This methodology is quasi-experimental and attempts to utilize historical performance as a reference with which to compare post-intervention performance. As such, the study will have both retrospective and prospective components. Children 18 months to 18 years of age who were admitted between January 1, 2005 and December 31, 2007 will be eligible for the retrospective portion of the study. These will be found by creating a database that includes all patients admitted to the hospital from the emergency department during this time period who meet our age criteria and have the *International Classification of Diseases, Ninth Revision* (ICD-9) diagnosis code of pneumonia (486) assigned in the admission diagnosis field. Patients less than 18 months of age will not be included in order to eliminate the majority of patients with bronchiolitis who might be misclassified as having pneumonia. All medical records will then be reviewed, and only patients who met pre-defined criteria for CAP will be included. For the purposes of the study, CAP will be defined as the presence of infiltrate on chest radiograph in addition to the presence of at least one of the following signs or symptoms in a patient who had not been hospitalized or residing in a long-term care facility within 14 days of admission: fever $\geq$ 100.4 degrees Fahrenheit, tachypnea (based on normal respiratory rates for age), or abnormal auscultatory findings on lung exam. Patients with known immunodeficiency, neutropenia (absolute neutrophil count <500 at the time of admission), or chronic medical conditions other than asthma, as well as infants born at less than 32 weeks gestational age and patients who were assigned an admitting diagnosis of bronchiolitis will be excluded.

The primary outcome of the retrospective portion will be length of stay Time to clinical stability [defined as first temperature <100.4 degrees F after last documented fever, age-appropriate respiratory rate, oxygen saturation >93% on room air, and able to take oral fluids (defined as not requiring intravenous fluid at a rate greater than needed to keep the vein open)] will be used as a secondary outcome. Adherence to proposed quality measures 1 through 5 as listed in table one will also be utilized as secondary outcomes. As this study is constructed to examine emergency department management, it is unlikely that transition to oral antibiotics will be seen over the ED stay. Transition from IV to po antibiotics will subsequently be excluded from the quality measures analysis.

Following the eligibility window for the retrospective portion of the study, a series of interventions will be made in the pediatric emergency department aimed at education of physicians, nurses, and clinical support staff on the proposed process measures for quality care in pediatric pneumonia. These interventions will occur between January 1, 2008 and January 31, 2008 and will consist of planned sessions dedicated to the management of pediatric pneumonia. An hour-long lecture for physicians will be taught by the principal investigator and will focus on general medical aspects of pneumonia in children. The final thirty minutes will educate physicians on the concept of quality measures and will outline the proposed five measures pertaining to ED care. Interns, residents, and attending physicians will then be strongly encouraged to promote adherence to these guidelines as a general measure of good clinical practice. Shorter meetings will also be held with nursing staff regarding quality measures and the necessity of oxygenation assessment and rapid administration of medications following a doctor's orders. These will be lead by nurse managers. Similar staff meetings will be held with phlebotomy and radiology staff in order to emphasize the need for rapid chest x-rays and blood cultures. Following these introductory meetings, monthly follow-up reminders will be included in staff meetings for the various departments. As a means to reinforce adherence to indicators in the clinical setting, all children triaged with a possible diagnosis of pneumonia will have a CAP worksheet placed in the front of their chart. For the purpose of this intervention, pneumonia will be defined as fever > 100.4F (or history of fever) and either tachypnea (dependent on age) or hypoxia (defined as oxygen saturation <93%). Although the group of children initially triaged as CAP and subsequently receiving the CAP worksheet will not exactly match the cohort of children formally diagnosed and treated for pneumonia (the study population), they will largely overlap and the worksheet will be utilized in the majority of patient used in the study.

The prospective portion of the study will extend from February 1, 2008 through January 31, 2010. Similar criteria for inclusion will be applied to those children in the prospective arm. Again, an ICD-9 admission diagnosis of pneumonia will be utilized to select the patient population in question. This diagnosis will then be confirmed with the specific criteria as outlined above. The same age requirements and exclusion parameters will apply to the prospective portion of the study. The primary and secondary outcomes will remain unchanged. Following completion of the prospective portion of the study, outcome measures will be compared between the retrospective and prospective arms. We hypothesize that the prospective group will show a statistically significant decrease in length of hospital stay and time to clinical stability and an increase in adherence to proposed process measures. Although we believe that length of hospital stay and time to clinical stability will be improved because of increased adherence to quality measures, other secular causes may influence change in these parameters over time. In order to address this, a "before and after" control condition will be utilized as marker for secular changes between the retrospective and prospective groups. For this study, we will utilize the average length of stay for asthma exacerbations in the same population with the same exclusion parameters. Asthma seems particularly appropriate for this function as its therapy has not changed significantly over the time frame in question.

Power Analysis:

An unpaired t-test was utilized for power analysis in this study. Although there are no clear data for expected length of stay in this population, most pediatric pneumonias have brief admissions of approximately 2 days (or 48 hours). The standard deviation is likely to be approximately one day (24 hours), with approximately 70% of children falling between 24 and 72 hours of hospitalization. From a previous retrospective investigation, we assume that adherence to quality measures (particular time to antibiotic administration) with cause a 25% reduction in hospital length of stay and 25% reduction in time to clinical stability in 50% of children.[15] Using the unpaired t-test, this corresponds to approximately 250 children needed in each cohort for 80% power, testing at $p=0.05$. It is estimated that approximately 150 children are admitted to CHONY each year with the diagnosis of pneumonia. As such, the study period has been set to encompass two years per arm.

Statistical Analysis:

Means and standard deviations will be calculated for length of stay in both the prospective and retrospective groups. These will be calculated in hours. As hospitalizations greater than 96 hours are likely to be accounted for by serious complications rather than simple non-adherence to quality measures in the ED, all admissions >96 hours in length will simply be reported as 96 hours during calculation. The student's t-test will utilize the means, standard deviations, and sample sizes of the prospective and retrospective cohorts in order to report a p value. Statistical significance is set at $p<0.05$. Similar calculations will be employed for the time to clinical stability and adherence to process measures.

C. Study Procedures:

D. Study Drugs: No study drugs will be employed apart from conventional antibiotics and other medications used in the treatment of CAP. These medications would be used in the absence of this research protocol and their risks are consequently not altered by the implementation of the study.

E. Medical Device: None.

F. Study Questionnaires: None.

G. Study Subjects: The inclusion and exclusion characteristics of study subjects are outlined above. We expect study subjects to grossly parallel the patient population at CPMC with 50% males and 50% females. Approximately 40% of subjects are expected to be Hispanic in origin, 30% Caucasian, 20% African American, and 10% Asian. Based on published demographics for pediatric pneumonia, we expect 60% of children to be <5 years in age.

H. Recruitment of Subjects: All patients admitted through the pediatric ED with the diagnosis of pneumonia will be considered for the study. No subjects will be formally recruited for the study as the enrollment process is automatic.

I. Confidentiality of Study Data: All medical records will be reviewed in a locked facility on-site at Columbia University Medical Center. Charts will be examined and pertinent data will be copied without identifying information onto previously designed work sheets. A "link field" coding system will be constructed should the data need to be reunited with its original medical

record. After all information has been collected, the data will be examined in its fully de-identified form using commercially available computer software.

J. Potential Conflict of Interest: None.

K. Location of the Study: Emergency Department, Children's Hospital of New York / New York Presbyterian Hospital, Columbia University Medical Center – New York City, New York

L. Potential Risks: The retrospective portion of the trial will pose no clinical risk to any human subjects involved. The only possible risk pertains to examination of protected health information. The use of personally identifiable confidential information will be confined to the data collection stage and all records with then be de-identified with the use of "link field" coding as outlined above. Although the prospective portion of the trial will involve implementation of medication treatment, those medications and procedures employed will be no different than current standard of care. As such, there will be no more than minimal change in risk from baseline clinical practice.

M. Potential Benefits: Patients enrolled in the prospective portion of the study may improve emergency room care with better adherence to proposed measures. Whether these measures will elicit clinically substantial improvements in health outcomes will be examined in the study. Larger benefits of the study include improving understanding on the role of quality measures and increasing attention to evidence-based practice in the treatment of CAP.

N. Alternative Therapies: N/A.

O. Compensation of Subjects: None.

P. Cost to Subjects: None.

Q. Minors as Research Subjects: Subpart D of 45CFR46 (HHS) and 21CFR50 (FDA) puts forth requirements used in the enrollment of minor subjects into medical research. The three areas considered under this heading relate to (1) risk/benefit analysis, (2) the permission of parents/guardians, and (3) assent of the child. Both the retrospective and prospective portions of this work will fall under Section 404 "research not involving more than minimal risk." Although there are risks associated with the treatment of CAP (e.g. medication side effects, procedural complications), there will be no alterations of these risks by implementation of the study. There is also no more than minimal risk associated with the data collected and utilized in the study. No sensitive diagnoses are being considered and all data will be de-identified early in the collection period. The study instrument involves education of clinical staff and the use of a worksheet outlining the proposed quality measures for the treatment of CAP in children. Although these have not been formally validated in the pediatric population, their implementation should, if anything, lead to better evidence-based care with potential clinical benefits. This project will be eligible for waiver of parental permission as (1) the study has no more than minimal risk, (2) a waiver of consent will not affect the rights and welfare of the study population, and (3) the research could not be practically carried out without the waiver. This last stipulation is grounded in the universal education on CAP quality measures provided to emergency department clinical staff. As these measures will have become standard of care in the emergency department, it is not feasible to decline participation in the implemented study while still receiving care at CHONY. Further, knowledge of study design and outcomes may make guardians concerned that participation in the trial would truncate length of stay. Such a perception could alter ultimate

length of hospitalization and research results. The only risk to participation involves data collection, as outlined in the confidentiality section above.

R. Radiation or Radioactive Substances: None.

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