Serum Procalcitonin Levels on Antibiotic Duration & Patient Outcomes in COPD Exacerbations

By

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Presented to

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Serum Procalcitonin Levels on Antibiotic Duration & Patient Outcomes in COPD Exacerbations

Chronic obstructive pulmonary disease (COPD) is defined as a chronic inflammatory response that leads to progressive damage and airflow impairment in the lungs (Global Initiative for Chronic Obstructive Lung Disease, 2013). It is a major cause of morbidity and mortality annually in the United States. According to the Centers for Disease Control (CDC, 2013b), COPD accounts for over 700,000 hospital admissions and is the third leading cause of death. Exacerbations are the leading cause of economic burden, morbidity and mortality in those individuals with COPD (GOLD, 2013).

COPD exacerbations requiring acute medical treatment are frequently encountered by providers within the intensive care unit (ICU). Most exacerbations are precipitated by bacterial or viral respiratory infections, environmental pollutants and other unknown factors (GOLD, 2013). Patients present to the hospital with worsening shortness of breath, increased sputum production and hypoxia. Treatment options according to the GOLD Guidelines include the use of bronchodilators, oxygen therapy, steroids and antibiotics. Many of the therapies used to treat COPD are fairly consistent among most providers with differences noted in duration of treatment and medication preference, however, antibiotic use in COPD exacerbations continues to be controversial. Evidence supports the use of antibiotics in those individuals who present with clinical signs of bacterial infections. However, causality of COPD exacerbations is lacking in approximately one-third of severe cases.

Overuse and misuse of antibiotic therapy has led to a surge of increasing antimicrobial resistance. Additionally, antibiotics have been labeled as the single most important factor leading to resistance worldwide (CDC, 2013a). According to the New England Health Institute (2011), antibiotic-resistant infections are responsible for $20 billion in excess health care costs and $8
million in hospital days. In order to reduce antibiotic use without compromising patient care, the development of rapid and accurate clinical testing is a surging area of clinical research. Serum biomarkers have been widely used for diagnosing, determining prognosis, and optimizing therapy strategies for many diseases. Their clinical use has been expanded to include the potential for guiding clinical management, particularly antibiotic therapy in conditions such as COPD exacerbations. Among those, procalcitonin (PCT) has been extensively studied with data supporting its use in diagnosing bacterial infections and potentially guiding antimicrobial duration (Soni et al., 2013). Serum PCT levels are primarily elevated in the presence of bacteria and noted to be more sensitive than other biomarkers in distinguishing a bacterial etiology (Fazili, Endy, Javaid, & Maksey, 2012). Additionally, levels are not affected by inflammatory disorders, viral infections or medications (Fazili et al., 2012).

Project Question and Objectives

In adult patients who presented to the ICU with a COPD exacerbation and a serum PCT level less than 0.25 ug/l, was there a difference in outcomes for individuals in which antibiotics were de-escalated or discontinued compared to patients who were continued on the usual care?

Project objectives were to examine:

- Whether a difference existed in antibiotic duration between individuals that were de-escalated or discontinued versus received usual care.
- Whether a difference existed in ventilator days between individuals that were de-escalated or discontinued versus received usual care.
- Whether a difference existed in ICU length of stay between individuals that were de-escalated or discontinued versus received usual care.
Review of Literature

Numerous studies have been done analyzing serum PCT levels as a guide to reduce antibiotic use in clinical practice. Study approach has primarily focused on elevated PCT measurements and the probability of bacterial infections for guidance of antibiotic duration (Schuetz et al., 2009). Most antibiotic stewardship studies have used similar treatment algorithms based on serum PCT cut-off ranges (Haubitz, Mueller & Schuetz, 2013). These cut-off ranges were developed based on observational studies, investigated, and then repeatedly validated in several randomized controlled trials and within various independent groups. Treatment recommendations within these studies were based on four classes: strongly discouraged, discouraged, encouraged, and strongly encouraged antibiotic use (Haubitz et al., 2013). Studies that evaluated serum PCT levels in respiratory infections used the cutoff range of 0.5 ug/l and 0.25 ug/l for strongly encouraged and encouraged antibiotic use, respectively. Values less than 0.25 ug/l and 0.10 ug/l discouraged and strongly discouraged the use of antibiotics.

Findings of several clinical studies have supported the use of serum PCT levels for reducing antibiotic duration without compromising patient outcomes. The first study to test the hypothesis of serum PCT levels and antibiotic duration was the ProRESP Trial (Albrich, Christ-Crain, Chastre, Shuetz, & Mueller, 2010). This study consisted of 243 patients initially seen in the emergency department with different respiratory infections such as community-acquired pneumonia (n = 87), COPD exacerbation (n = 60), acute bronchitis (n = 59), asthma (n = 15), and other respiratory infections (n = 24) (Christ-Crain et al., 2004). Patients were admitted to the hospital or followed up as an outpatient for data collection. Results of the ProRESP Trial indicated a reduction of antibiotic use in the PCT group without compromising outcomes.
Duration of antibiotic treatment in the PCT group was reduced by approximately two days in all patients with respiratory infections. Additionally, patients with COPD exacerbations had a 49% reduction of antibiotic use with no statistical significance in ICU stay, rate of post-study exacerbations or post-study readmissions when compared to the usual care group (Christ-Crain et al., 2004).

Stolz et al. (2007) conducted a study of 208 patients with acute COPD exacerbations. Patients were followed during the hospitalization, at a follow-up visit and throughout 6 months post-hospitalization. Baseline characteristics were similar in both the PCT and usual care group with the majority of patients severity of COPD classified as GOLD stage III or IV. Results indicated a reduction of antibiotic prescription rates to 40% versus 72% in the PCT and usual care group, respectively. Additional results revealed that subsequent antibiotic use for the treatment of an acute exacerbation within six months did not differ between the two groups and the PCT group had a sustained reduction in antibiotic exposure for up to six months (Stolz et al., 2007). Furthermore, there was no difference in mean days to the next exacerbation in the PCT and usual care group, 70.0 days versus 70.4 days. The authors also note there was no difference in the rate of re-hospitalizations for COPD exacerbations in either group (Stolz et al., 2007).

Evidence from earlier clinical trials suggested promising clinical value of PCT guided algorithms to reduce antibiotic use, however, each trial had relatively small sample sizes limiting its power. The ProHOSP Trial was a randomized controlled trial that evaluated 1359 patients from six hospitals (Schuetz et al., 2009). The objective of this trial was to evaluate the clinical usefulness of PCT guided algorithms on a larger patient scale without compromising patient outcomes. Results from the ProHOSP Trial revealed that the PCT guided group did not have a higher risk of adverse outcomes compared to the usual care. In addition, overall mean duration of
antibiotic exposure and use was less in the PCT group. Significant differences in antibiotic exposure were noted in COPD exacerbations and acute bronchitis, a difference of 21.2% and 26.8%, respectively (Schuetz et al., 2009). Hospital length of stay was similar in both groups at 9.4 days in the PCT group and 9.2 days in the usual care group.

Schuetz et al. (2011) conducted a systematic review that included 14 randomized controlled trials that investigated PCT algorithms for antibiotic duration and treatment. A total of 4467 patients were included in the systematic review. Six of the studies, including 2449 patients, analyzed respiratory infections in the hospitalized setting. Pneumonia, COPD exacerbations, and acute bronchitis were the most commonly treated respiratory infections in the six studies reviewed (Schuetz et al., 2011). Results indicated a reduction in prescription rates and in antibiotic duration. All six trials indicated no significant difference in mortality in the PCT versus usual care group. According to Schuetz et al. (2011), several limitations existed among all 14 studies including issues with provider adherence, algorithm differences among studies, and research being primarily embedded within the European setting.

The Agency for Healthcare Research and Quality (2012) published a review of the evidence on serum PCT levels and its clinical usefulness in different disease states and patient populations. A high evidence rating was given to serum PCT levels reducing antibiotic duration and prescription rates in respiratory infections and a moderate evidence rating suggested serum PCT levels did not increase mortality, hospital length of stay, or ICU admission rates (AHRQ, 2012). At present no evidence-based guidelines have been developed based on current research. However, some hospitals have begun to initiate clinical algorithms based on evidence to assist the clinician in antibiotic management for patients who present with respiratory infections. For
example, The Nebraska Medical Center has designed an initial and follow-up clinical algorithm based on research studies of serum PCT levels and antibiotic management.

Conclusions based on current literature and evidence support the use of serum PCT levels for the reduction of antibiotic use without compromising clinical outcomes in COPD exacerbations. The above studies repeatedly demonstrated a decrease in antibiotic duration or prescription rates and no adverse outcomes in length of stay, readmission rates or mortality rates when compared to usual care. Furthermore, Schuetz et al. (2009) indicated a 30% reduction in antibiotic associated side effects in the PCT guided group. A major limitation to most of the studies was the lack of provider adherence. However, despite a 41% non-adherence rate in one trial a 25% reduction in antibiotic therapy was still observed (Albrich et al., 2010).

**Theoretical Framework**

The theoretical framework used was the Iowa Model for Evidenced-Based Practice found in Appendix A. The Iowa Model is a multiphase process that provides guidance for decision-making to affect patient and system outcomes (Melnyk & Fineout-Overholt, 2011). A knowledge focus trigger serves as the catalyst for practice improvement and change (Titler et al., 2001). Information within the literature on serum PCT levels and antibiotic stewardship in respiratory infections is the trigger for a potential change in practice. A thorough review of the literature has indicated sufficient enough data to evaluate whether a difference exists in outcomes among COPD patients who receive a change in antibiotic treatment compared to usual care. According to the literature, serum PCT levels have reflected a positive change in practice without compromising clinical outcomes. The process of de-escalation or discontinued antibiotic use in COPD patients with a serum PCT level less than 0.25 ug/l was compared to COPD patients who
Serum Procalcitonin Levels

were continued on the usual antibiotic regimen. Outcomes in length of stay, antibiotic duration and ventilator days were evaluated to determine the need for a change in practice.

Methods and Procedures

Project Design

A comparative descriptive design was used to examine and describe the differences in COPD patients who received a change in antibiotic treatment versus usual care. This design is found in Appendix B.

Study Population and Sampling Plan

The population was all adult patients who presented to the ICU diagnosed with a COPD exacerbation. The initial serum PCT level was less than 0.25 ug/l and was drawn on presentation or within 12 hours of being admitted. All patients were started on antibiotic therapy at the time of admission.

Patients were ineligible if they had received a diagnosis of sepsis or pneumonia on admission or anytime during the hospitalization. Additional exclusions were all patients who had a history of interstitial lung disease such as pulmonary fibrosis, severe immunosuppression other than chronic steroid use and chronic diseases that necessitated chronic antibiotic therapy.

Patient sampling consisted of retrospective data collection for all patients who met criteria from January 2013 to December 2013 within two ICUs in a single center tertiary hospital. Purposive sampling was the method of selection for all patients who met eligibility criterion.

In order to obtain the sample, a database was searched for all patients who were admitted to the ICU with a diagnosis of a COPD exacerbation. Patient data was extracted and transferred to a spreadsheet to undergo chart review. Each patient’s chart was reviewed to ensure all
criterion were met. If criterion were met each patient was transferred to a second spreadsheet for extraction of additional study information. All patient information was de-identified. Data collection was completed by a nurse practitioner trained in both databases and the electronic medical record utilized by the hospital.

The project time frame was June 2014 to August 2014 for data collection and September 2014 to October 2014 for data analysis. IRB approval was obtained prior to data collection (see Appendix C). Involved players included a large tertiary hospital, nurse practitioner and nursing analyst.

**Measurement Methods**

Measurement methods were a retrospective chart review of existing healthcare data that included serum PCT levels, assessment of antibiotic duration, de-escalation or discontinuation of antibiotics versus continuation of usual care, ICU length of stay and number of ventilator days.

Serum PCT measurements were based on values previously described in multiple studies that had repeatedly validated its use. Peak levels were noted to occur within 12-48 hours (Gilbert, 2010). Therefore, all serum PCT measurements extracted were drawn on admission or within 12 hours.

**Data Collection Plan**

Prior to data collection two excel spreadsheets were developed. The first included all patients with a COPD exacerbation and all eligibility criteria (see Figure D1 and D2). All patients who met eligibility criteria were transferred to the second excel spreadsheet. The second spreadsheet included all primary outcomes such as antibiotic duration in both groups, ICU length of stay and ventilator days (see Figure E1). In addition, antibiotics were further assessed by type for those who received a broad spectrum antibiotic such as Zosyn compared to those de-escalated
to a narrow spectrum antibiotic such as Vancomycin or discontinued on antibiotic therapy. Patients were separated to the treatment or usual care group based on antibiotic discontinuation. According to the GOLD Guidelines (2014), antibiotic duration is usually recommended for five to ten days. Therefore, patients included in the treatment group had antibiotics de-escalated or discontinued in four days or less versus the usual care group who received antibiotics for five days or greater.

Secondary data was collected on demographic variables such as age, gender, and smoking status. Co-morbidities such as diabetes mellitus, chronic kidney disease, coronary artery disease, obstructive sleep apnea and congestive heart failure were documented (see Figure E2). More in depth data was collected on the patient’s COPD status such as their GOLD stage, chronic home O2 use and COPD maintenance medications (i.e. inhaled steroids, anticholinergics, and B2-agonists) (see Figure E3). Many of these variables were documented in previous studies to ensure a degree of homogeneity among the sample sizes and for secondary correlations. Patients received care from one of six providers while in the ICU. Providers were labeled to each encounter to assess whether specific providers de-escalate, discontinue or continue with usual care compared to another provider.

Data Analysis Plan

Statistical analysis was completed using SPSS software, version 22. Descriptive statistics were performed on all demographic variables such as gender and smoking status, co-morbidities, and COPD status such as chronic home oxygen use and COPD maintenance therapy. The primary endpoints of antibiotic duration, ICU length of stay, and ventilator days were analyzed using the nonparametric Mann-Whitney U test at a 95% confidence. The Chi Square Automatic Interaction Detection (CHAID) Model was used to identify secondary endpoints and predict
potential important differences in patient attributes between those in the usual versus de-escalated or discontinued care group.

**Results**

A total of 478 patient encounters were identified as having a potential indication for study inclusion. Search terms such as acute respiratory failure, acute on chronic respiratory failure, chronic respiratory failure and COPD exacerbation were used for recruitment. Of those encounters, 463 were included on the first spreadsheet of eligible criteria. Of these, 107 encounters (23%) were identified as having a COPD exacerbation for admittance to the ICU. Twenty-one (19.6%) patient encounters were identified as having met all inclusion criteria and transferred to the second spreadsheet for further data collection.

Baseline characteristics were collected on all demographic variables, co-morbidities and COPD status (see Appendix F, Table 1). The mean age was 62 years with ages ranging from 45-74 years. Men represented approximately 57% whereas women 43%. Patients who currently smoked represented 47.6% of the COPD exacerbations, 38.1% were former smokers, and 14.3% had no smoking history. Diabetes mellitus and congestive heart failure had similar representation for those identified as having the diagnosis versus those with no diagnosis. The majority of the patients were identified as not having chronic kidney disease, coronary artery disease, or obstructive sleep apnea. Chronic home oxygen use was documented in 61.9% and COPD maintenance therapy was noted in 81% of the patients. GOLD staging was not identified in 95% of the patients.

**Primary Outcomes**

In a Mann-Whitney U test at 95% confidence, there was a significant difference (p = 0.000) in antibiotic duration in the usual care group, with a mean rank of 17 antibiotic duration
days (n=9) as compared to the significantly lower mean rank of 6.5 antibiotic duration days 
(n=12) in the de-escalated/discontinued care group (see Figure G1). The mean rank in ICU 
length of stay and ventilator days were higher in the de-escalated/discontinued care group 
compared to the usual care group, however, these differences were not significant (p = 0.247 and 
p = 0.422, respectively) (see Figure G2 and G3).

Secondary Outcomes

In a CHAID model predictive of usual care versus de-escalated or discontinued care, 
antibiotic duration, smoking status, and chronic home oxygen use demonstrated a significant 
interaction. These three variables demonstrated that there are potentially important differences 
between usual care versus de-escalated or discontinued care, in terms of patient attributes or 
outcomes. The remaining variables did not predict any significant interaction. The CHAID 
model utilized the Bonferroni method to adjust the p-values to avoid over-reading of significance 
associated with having multiple comparisons.

Discussion

Causes of COPD exacerbations are precipitated by various factors. The most common 
causes are bacterial or viral respiratory infections. Studies have indicated at least 50% of all 
patients who present with a COPD exacerbation have bacteria in their lower airways (GOLD, 
2014). However, a large portion of these patients also have bacteria colonizing their airways in 
the stable phase of COPD. Interestingly, approximately one-third of all severe COPD 
exacerbations cannot be attributed to an identifiable cause (GOLD, 2014). Often times, diagnosis 
of an exacerbation relies on the patient’s clinical presentation of an acute change beyond their 
normal variations. Antibiotics are frequently prescribed during an exacerbation and treatment 
length is usually 5-10 days, although an Evidence D recommendation (GOLD, 2014).
Overuse of antibiotics is the leading cause of antibiotic resistance. The CDC (2013) estimates that more than two million are sickened with antibiotic resistant infections each year, with at least 23,000 dying as a result of these infections. Appropriate use of antibiotic prescriptions are vital in order to reduce antibiotic-resistant rates and cut cost. Use of biomarkers, such as procalcitonin, have shown promise for delineating patients who potentially do not need antibiotics or can be de-escalated/discontinued off the antibiotic regimen. Previous studies have indicated procalcitonin as an effective part of antibiotic stewardship for the reduction of antibiotic use without effecting outcomes negatively.

This project mimics results found in prior studies. In patients who received fewer days of antibiotic therapy based on guideline recommendations and serum procalcitonin levels less than 0.25 ug/l, no significance difference was noted in the primary outcomes of ICU length of stay or ventilator days. However, duration of antibiotic use was noted to be significantly different in the treatment group, a frequently noted aspect when using serum procalcitonin levels in aiding diagnosis and antibiotic stewardship. Interestingly, a significant interaction was noted between usual care compared to de-escalated/discontinued care for smoking status and chronic home oxygen use. However, the data collected was nominal level allowing for a relationship to be acknowledged but no correlation formulated.

Several limitations exist within this project. The small sample size is a major limitation and each group is at the lower limit for statistical analysis to be conducted. A recommendation for the future or follow-up similar to this study, would be to increase the sample size of each group. Additionally, interactions may appear more significant as a result of the small sample size, therefore, increasing group size may reveal a more predictive relationship between variables. Additional limitations were extensive use of nominal level data, missing variables, and
the procalcitonin collection time-frame. The extensive use of nominal data while appropriate for the small sample size would limit the amount of knowledge or ability to assess correlations that may be more apparent in larger samples. Variables such as GOLD Stage and provider discontinuation were unavailable or difficult to identify within the EMR. The procalcitonin collection time-frame was indicated as drawn on admission or within 12 hours, however, literature states that levels peak between 12-48 hours. By not allowing the inclusion of the additional hours, participants were ineligible even if all other criterion had been met. Lastly, there were inconsistencies in ordering the test. Of the remaining 86 patients who were diagnosed with a COPD exacerbation but not included in the study, 36% did not have a serum procalcitonin level collected.

**Implications**

This project adds to the growing body of literature favoring the use of procalcitonin as an aid to antibiotic stewardship. With evidence supporting its use, serum procalcitonin levels can potentially prove useful in identifying patients with a lower probability of a bacterial infection and limiting antibiotic use. Future direction for clinicians is the potential development of an algorithm utilizing procalcitonin levels and trends as a mean to initiate or discontinue antibiotic therapy in conjunction with additional evidence-based management. Furthermore, DNP prepared clinicians who frequently encounter patients with COPD exacerbations can use the findings identified within these studies to change practice within their own clinical setting. It is a great opportunity to engage in an evidence-based practice project or simply review data prior and after implementation with a select few in the COPD population. The clinical value associated with procalcitonin use has the potential to reduce inappropriate antibiotic use, decrease antibiotic resistant infections, and reduce cost of treatment.
Many studies cite the reduction of antibiotic days but little research has indicated how the use of serum procalcitonin effects cost of care. According to Perera, Armstrong, Sherrill, and Skrepnek (2012), the mean cost of hospitalized care for patients with a COPD exacerbation was $11,195 with median costs of $7110 in 2010. Determining the cost incurred secondary to antibiotic therapy would be beneficial for understanding the potential cost containment that may be achieved with a procalcitonin-guided algorithm. Additionally, the reduction of antibiotic use could impact secondary outcomes such as reducing antibiotic-resistant infections and the cost associated with care of these infections. However, cost must be considered for the equipment and test use.

**Conclusion**

In conclusion, the project findings supported those found within the literature. Previous studies suggest serum procalcitonin levels as an effective biomarker for antibiotic stewardship without the development of poor outcomes. This project supported the evidence with data that showed a decrease in antibiotic duration without a significant variation between the treatment and usual care group in ICU length of stay and ventilator days. However, there are no large scale studies to date that analyze outcomes of procalcitonin levels in COPD exacerbations solely admitted to the ICU. Further research with large sample sizes within the ICU are needed.
References


Appendix A

Research Triggers to Improve Practice Through

Problem Focused Triggers
1. Risk Management Data
2. QA/QI Data
3. Identification of clinical problem
4. TQM/CQI

Knowledge Focused Triggers
1. National agencies or organizational standards & guidelines
2. Philosophies of care
3. Questions from institutional standards
4. New information in the literature

Assemble relevant research literature

Critique & evaluate for use in practice

Yes

Is there a sufficient research base?

Research base is sufficiently developed to guide practice
1. Select outcomes to be achieved
2. Design nursing/multidisciplinary practice
3. Implement practice changes on a pilot unit
4. Evaluate process and outcomes
5. Modify intervention as needed

No

Research base not sufficiently developed to guide practice

Conduct Research
Consult with experts
Determine scientific principles

Is the change appropriate for adoption in practice?

Change practice

Monitor Outcomes

Patient & Family
Staff
Fiscal

Figure 1. Iowa Model for Evidenced-Based Practice
Appendix B

Figure 2. Comparative Descriptive Design for COPD exacerbations and serum PCT levels to compare antibiotic duration and patient outcomes.
Appendix C

STUDY APPROVAL NOTIFICATION

Serum Procalcitonin Levels on Antibiotic Duration and Patient Outcomes in COPD Exacerbations

Sponsor: MHS / Essence Carter-Griffin

Protocol Number: 2014.00.658.A
May 25, 2014

The new study listed above was reviewed and approved through expedited review July 18, 2014 by Rebecca M. Clark, BBA, Aspire IRB Board Member. This study was approved at that time with no additional restrictions added to the conduct of the study.

Essence M. Carter-Griffin, MSN, RN, ACNP-BC, was approved to conduct this study at the following locations:

Methodist Dallas Medical Center
1441 N. Beckley Ave.
Dallas, TX 75203

Methodist Health System Clinical Research Institute
1411 N. Beckley Ave., Pavilion III, Suite 168
Dallas, TX 75203

It has been determined that Informed Consent for this study is not necessary and the requirement has been waived.

The IRB has determined that your study is Minimal risk, and assigned an approval period of Annual review. Your approval period ends on July 17, 2015; as a reminder, you will receive a Research Status Report Form approximately sixty days prior to this date.

The Principal Investigator is responsible for providing the IRB with the necessary materials for re-approval by the due date provided on the application. This form must be received by the due date to allow ample time for adequate review prior to the study's expiration date. Missed submissions are the responsibility of the Principal Investigator regardless of whether or not the IRB notifies you.

Version dated January 2014 - Aspire IRB
Appendix C

The continuation of research after expiration of IRB approval is a violation of the regulations governing research.

It is required that Aspire IRB be notified of:

- All amendments or changes to the protocol
- Changes to the protocol that are implemented without prior IRB approval to eliminate an apparent immediate hazard to subjects (must be reported within 24 hours of implementation)
- Unanticipated problems involving risks to subjects or others (within 10 calendar days of discovery). This includes protocol deviations that fit the criteria for an unanticipated problem.
- All material used to recruit study subjects (prior IRB approval is required before use)
- Any other changes in the research activity

The Principal Investigator may not make any changes in the research, without prior approval of Aspire IRB, except when necessary to eliminate immediate risk to study subjects. In addition, it is the responsibility of the Principal Investigator to uphold the following three ethical principles outlined in the Belmont Report during the conduct of this study:

  o Respect for persons: individuals should be treated as autonomous agents and persons with diminished autonomy are entitled to protection.
  o Beneficence: maximize possible benefits and minimize possible harms.
  o Justice: benefits and burdens of research should be distributed equally.

Aspire IRB is duly constituted and has written procedures in compliance with requirements defined in 21 CFR Parts 50 and 56, 312, 812, 45 CFR 46 and ICH Guidelines relating to Good Clinical Practice. Aspire IRB's mission is to ensure that research is conducted ethically according to the principles of the Belmont Report and in compliance with federal regulations, international regulations, ICH Guidelines for Good Clinical Practice, applicable state and local laws, Aspire IRB Standard Operating Procedures, and that the rights and welfare of human subjects are protected.

Charlotte Stewart, CIP, Chief Operating Officer  
7-22-14  
Date
Appendix D

Eligible Criteria

<table>
<thead>
<tr>
<th>Med. Record Num.</th>
<th>Numerical Code</th>
<th>COPD exacer.</th>
<th>ICU adm.</th>
<th>PCT level &lt; 0.25</th>
<th>PCT level w/ 12 hrs</th>
<th>On abx</th>
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</tbody>
</table>

**The above questions will be answered with yes or no**

If receives all yes under eligible criteria and all nos under ineligible criteria then pt will be highlighted green and placed on the next spreadsheet.

*Figure D1.* Initial spreadsheet used to collect data on patients for potential study inclusion. Part one of a two-part process to be eligible for additional data collection. COPD exacerb. = COPD exacerbation; ICU adm. = ICU admission; PCT = procalcitionin; abx = antibiotic
Appendix D

<table>
<thead>
<tr>
<th>Ineligible Criteria</th>
<th>Sepsis</th>
<th>Pneumonia</th>
<th>ILD</th>
<th>Immunosuppr.</th>
<th>Chronic abx</th>
</tr>
</thead>
</table>

*Figure D2. Initial spreadsheet used to collect data on patients for potential study inclusion. Part two of a two-part process to be eligible for additional data collection. ILD = Interstitial Lung Disease; Immunosuppr = immunosuppression; abx = antibiotic.*
### Appendix E

**Data Collection**

<table>
<thead>
<tr>
<th>Primary Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abx duration</td>
</tr>
</tbody>
</table>

**Numerical Code**

**Key**
- Abx duration = specified in days
- ICU LOS = specified in days
- Ventilator days = specified in days
- Abx type = broad versus narrow
- Treatment group = specify is pt de-escalated or discontinued on abx
- Usual care = yes or no

*Figure E1.* Second Spreadsheet for final data collection on all patients who met eligibility criteria. Sheet 1 of 2. Abx = antibiotic; LOS = length of stay.
Appendix E

<table>
<thead>
<tr>
<th>Data Collection</th>
<th>Demographic variables</th>
<th>Co-morbidities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Gender</td>
<td>DM</td>
</tr>
<tr>
<td>Gender</td>
<td>Smoking Status</td>
<td>CKD</td>
</tr>
<tr>
<td>Smoking Status</td>
<td></td>
<td>CAD</td>
</tr>
<tr>
<td>Key</td>
<td></td>
<td>CHF</td>
</tr>
<tr>
<td>Key</td>
<td></td>
<td>OSA</td>
</tr>
</tbody>
</table>

**Figure E2.** Second Spreadsheet for final data collection on all patients who met eligibility criteria. Sheet 2 of 2. DM = diabetes mellitus; CKD = chronic kidney disease; CAD = coronary artery disease; CHF = congestive heart failure; OSA = obstructive sleep apnea.
### Appendix E

**Figure E3.** Second Spreadsheet for final data collection on all patients who met eligibility criteria. Remaining data collected as part of Sheet 2 of 2.

<table>
<thead>
<tr>
<th>COPD Status</th>
<th>Provider</th>
</tr>
</thead>
<tbody>
<tr>
<td>GOLD Stage</td>
<td>Chronic home O2</td>
</tr>
</tbody>
</table>

**Key**

- GOLD Stage = specified as I, II, III, IV
- Chronic home O2 = specified as yes or no
- COPD main. Therapy = specified as inhaled steroids, B2 agonists, and/or anticholinergics

**Provider**

- Tran, Thomas, Wood
- Melissa, Monee', Nokie
### Appendix F

Table 1

**Baseline Characteristics of Patients in the De-escalated/Discontinued and Usual Care Group**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Treatment Care Group (n = 12)</th>
<th>Usual Care Group (n = 9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>60.3 (45-74)</td>
<td>64.6 (55-73)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>6 (50%)</td>
<td>6 (67%)</td>
</tr>
<tr>
<td>Female</td>
<td>6 (50%)</td>
<td>3 (33%)</td>
</tr>
<tr>
<td>Smoking Status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>7 (58%)</td>
<td>3 (33%)</td>
</tr>
<tr>
<td>Former</td>
<td>2 (17%)</td>
<td>6 (67%)</td>
</tr>
<tr>
<td>Never</td>
<td>3 (25%)</td>
<td>NA</td>
</tr>
<tr>
<td>Co-morbidities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>5 (42%)</td>
<td>6 (67%)</td>
</tr>
<tr>
<td>Chronic Kidney Disease</td>
<td>2 (17%)</td>
<td>1 (11%)</td>
</tr>
<tr>
<td>Coronary Artery Disease</td>
<td>1 (8%)</td>
<td>2 (22%)</td>
</tr>
<tr>
<td>Congestive Heart Failure</td>
<td>6 (50%)</td>
<td>5 (56%)</td>
</tr>
<tr>
<td>Obstructive Sleep Apnea</td>
<td>2 (17%)</td>
<td>1 (11%)</td>
</tr>
<tr>
<td>GOLD Stage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GOLD Stage 1</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>GOLD Stage 2</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>GOLD Stage 3</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>GOLD Stage 4</td>
<td>NA</td>
<td>1 (11%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>12 (100%)</td>
<td>8 (89%)</td>
</tr>
<tr>
<td>Chronic Home O2 Use</td>
<td>6 (50%)</td>
<td>7 (78%)</td>
</tr>
<tr>
<td>COPD Maintenance Therapy</td>
<td>10 (83%)</td>
<td>7 (78%)</td>
</tr>
</tbody>
</table>

*Note. GOLD = Global Initiative for Chronic Obstructive Lung Disease*
Appendix G

Type of treatment received

Usual Care | De-escalated/Discontinued
--- | ---
12 | ** p = 0.000

![Graph showing duration of antibiotic therapy](image)

Figure G1. Duration of antibiotic therapy in patients who received usual care (n = 9) versus de-escalated/discontinued care (n = 12). ** p = 0.000, indicating a significant difference (p < 0.05).
Appendix G

Type of treatment received

<table>
<thead>
<tr>
<th>Usual Care</th>
<th>De-escalated/Discontinued</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>p = 0.247</strong></td>
</tr>
<tr>
<td>Frequency</td>
<td>Frequency</td>
</tr>
<tr>
<td>12</td>
<td>8</td>
</tr>
<tr>
<td>10</td>
<td>6</td>
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<td>8</td>
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</tr>
<tr>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

Figure G2. ICU length of stay of patients who received usual care versus de-escalated/discontinued care. **p = 0.247, indicating no significant difference (p > 0.05).
Appendix G

**Figure G3.** Number of ventilator days for patients who received usual care (n = 9) versus de-escalated/discontinued care (n = 12). **p = 0.422**, indicating no significant difference (p > 0.05).