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Total Duration of Antimicrobial Therapy in Veterans Hospitalized With Uncomplicated Pneumonia: Results of a National Medication Utilization Evaluation

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Conflict of Interest Disclosures

Karl Madaras-Kelly is employed full time by Idaho State University and has a Without Compensation Appointment as a Clinical Pharmacist at the Boise VA Medical Center. He receives grant support unrelated to this work through the Dept. of Veterans Affairs sub-contracted to Idaho State University. He reports no conflict of interest.

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Abstract:

Objective: Practice guidelines recommend the shortest duration of antimicrobial therapy appropriate to treat uncomplicated pneumonia be prescribed to reduce the emergence of resistant pathogens. A national evaluation was conducted to assess the duration of therapy for pneumonia.

Design: Retrospective Medication Utilization Evaluation.

Setting: Thirty Veterans Affairs Medical Centers.

Patients: Inpatients discharged with a diagnosis of pneumonia.

Measurements: A manual review of electronic medical records of inpatients discharged with uncomplicated community-acquired pneumonia (CAP) or healthcare-associated pneumonia (HCAP) was conducted. Appropriate CAP therapy duration was defined as at least 5 days, and up to 3 additional days beginning the first day the patient achieved clinical stability criteria; the appropriate HCAP therapy duration was defined as 8 days. The duration of antimicrobial therapy for intravenous (IV) and oral (PO) inpatient administration, PO therapy dispensed upon discharge, *Clostridium difficile* infection (CDI), hospital readmission, and death rates were measured.

Results: Of 3881 pneumonia admissions, 1739 met inclusion criteria [CAP (n=1195); HCAP (n=544)]. Overall, 13.9% of patients [CAP (6.9%), HCAP (29.0%)] received therapy duration consistent with guideline recommendations. The median (IQR) days of therapy were 4(3,6), 1(0,3), and 6 (4,8) for inpatient IV, inpatient PO, and outpatient PO antimicrobials. CDI was rare

but more common in patients who received therapy duration consistent with guidelines. Therapy duration was not associated with the readmission or mortality rate.

Conclusions: Antimicrobials were commonly prescribed for a longer duration than guidelines recommend. The majority of excessive therapy was completed upon discharge, identifying the need for strategies to curtail unnecessary use post-discharge.

Introduction

Pneumonia is the leading inpatient infectious diagnosis for which antimicrobials are prescribed in the United States.[1] Supported by moderate to high quality evidence, guidelines produced jointly by the Infectious Diseases Society of America (IDSA) and American Thoracic Society (ATS) recommend treating pneumonia with the shortest appropriate duration of antimicrobial therapy to minimize risk for antimicrobial-related adverse events.[2-4]

Evidence supports short duration of therapy for treatment of uncomplicated pneumonia.[3-12] IDSA/ATS guidelines state, "patients with CAP [community-acquired pneumonia] should be treated for a minimum of 5 days (level 1 evidence), should be afebrile for 48-72 hours, and should have no more than 1 CAP-associated sign of clinical instability … before discontinuation of therapy (level II evidence). (Moderate recommendation.) A longer duration of therapy may be warranted if initial therapy was not active against the identified pathogen or if it was complicated by [abscess, empyema, severe immunosuppression, or] extra-pulmonary infection such as meningitis or endocarditis. (Weak recommendation; level III evidence)."[3] Recommended therapy duration for patients with uncomplicated healthcare associated pneumonia (HCAP) who respond to initial therapy is 7 to 8 days unless Gram-negative non-fermenting rods or complications are identified (level I evidence).[4]

Within the Veterans Health Administration (VHA), the Antimicrobial Stewardship Taskforce (ASTF) was created to optimize care by developing, deploying, and monitoring a national-level strategic plan for antimicrobial therapy management improvements.[13,14] While single-center studies have found antimicrobial therapy for CAP being frequently prescribed for

longer than recommended, the reproducibility of this finding across different facilities has not been assessed.[15,16] The ASTF collaborated with the VHA Center for Medication Safety to assess total duration of antimicrobial therapy prescribed for veterans hospitalized with uncomplicated pneumonia.[17]

Methods

This retrospective multicenter evaluation was conducted in 30 VHA facilities which volunteered to participate in this project. Inpatients discharged with a primary International Classification of Diseases, Ninth Revision Clinical Modification (ICD-9CM) diagnosis code for pneumonia (or pneumonia diagnosis secondary to primary sepsis diagnosis) during 2013 were evaluated.[18] Diagnoses, admissions, and patient demographics were identified using VA integrated databases through the Austin Integrated Technology Center. Up to 200 admissions per facility were randomly selected for review. Clinical pharmacists at each facility performed manual record reviews utilizing a standardized protocol and collection form. Completed cases were uploaded to a central database for analysis. Standardized chart abstraction was facilitated by detailed instructions, a data dictionary, and monthly conference calls.

Inclusion criteria required patient admission to any Medical ward including intensive care unit (ICU) wards for ≥48 hours, receipt of >24 hours inpatient antimicrobial therapy (e.g., at least 2 doses of a q24 hour antibiotic), documentation of pneumonia discharge diagnosis, and survival until discharge. Exclusion criteria were: complicated pneumonia (lung abscess, necrotizing pneumonia, thoracentesis performed); significant immunosuppression (cancer chemotherapy or absolute neutrophil count < 1500 cell/mm^3 within 28 days, organ

transplantation, HIV infection); or extra-pulmonary infection (e.g., meningitis, endocarditis).[3] Patients were also excluded if directly transferred from another inpatient facility; pneumonia occurred > 48 hours after admission; index hospitalization was > 14 days; previously hospitalized within 28 days prior to index admission; or discharged without documentation of completing a full course of therapy. In addition, patients who received initial therapy discordant with culture and susceptibility findings, were not clinically stable by discharge, or had Gram-negative non-fermentative bacilli cultured were excluded from analysis because according to the guidelines, either data is lacking to support a short duration of therapy such as initial discordant therapy, or a longer duration of therapy may be warranted such as Gram-negative non-fermentative bacilli and clinical instability at discharge.[4] Our intent for these exclusions was to minimize bias against clinician decision making for cases where a longer duration of therapy may have been appropriate.

Patients meeting all criteria had the following abstracted: demographics; prior healthcare exposures; admitting location (ICU or non-ICU ward); parameters for calculation of pneumonia severity (PSI) index; culture results obtained ≤ 48 hours of admission; duration of antimicrobials administered during hospitalization and prescribed upon discharge (or recommendations for outpatient duration in the Discharge Summary for patients receiving medications from non-VA sources); daily clinical stability assessment; *Clostridium difficile* infection (CDI) test results; and readmission or death within 28 days of discharge.[19]

Guideline similar CAP therapy duration was defined as a minimum of five days of antimicrobials, up to a maximum of three additional days beginning the first day the patient

was afebrile and exhibited ≤ 1 sign of clinical instability (HR > 100 BPM, RR > 24 BPM, SBP < 90, O2Sat < 90% or pO2 < 60 mmHg on room air or baseline O2 requirements, or not returned to baseline mental status).[3] This definition was made by consensus decision of the investigators and was necessary in order to operationalize the relationship between clinical stability and appropriate duration of therapy. Guideline similar HCAP therapy duration was defined as 8 days.[4] CDI was defined in accordance with VA criteria for hospital onset and community onset-healthcare-facility associated CDI.[20] All-cause hospital readmission and all-cause death were defined as inpatient readmission or any death, respectively, within 28 days after discharge for the pneumonia admission.

Demographics, comorbidities, microbiology results, antimicrobial utilization, CDI, readmission, and death rates between guideline similar and guideline excessive duration of antimicrobial therapy groups were characterized with descriptive statistics, Mann-Whitney U test, or Chi-Square test as indicated (significance defined as $P<0.05$). Multivariable logistic regression [SAS 9.3 (SAS Software, Cary, NC)] was used to assess association between duration of therapy exceeding recommended guidelines with all-cause readmission and all-cause death after adjustment for pertinent covariates. Odds ratios (OR) with 95% confidence intervals (± 95% CI) were reported. This medication utilization evaluation (MUE) was reviewed by the Hines VHA Institutional Review Board (IRB) for Human Subjects Protection. Based on VHA Policy Handbook 1058.05 which defines operations activities that may constitute research, the board determined that the evaluation constituted quality improvement rather than research, thus, was exempt from VHA Human Subjects Research requirements.

Results

3881 admissions were eligible for chart review. After manual chart review of inclusion and exclusion criteria, 1739 (44.8%) patients were available for duration of therapy analysis. (Figure 1) Only one admission for each patient was analyzed.

The cohort was comprised primarily of elderly male patients (96.6%) of whom more than two-thirds were hospitalized for CAP. (Table 1) Most patients had significant disease severity as indicated by PSI score; however, only 12% were directly admitted to the ICU. Blood cultures were collected in >95% of cases; lower respiratory cultures were obtained in 39.9% of cases.

Commonly administered antimicrobials during hospitalization and at discharge are summarized in Table 2. Anti-pseudomonal β-lactams and anti-MRSA antimicrobials were more frequently administered to patients with HCAP while 3rd generation cephalosporins and macrolides were more likely to be administered to patients with CAP. Fluoroquinolones were prescribed to 55.3% of patients upon discharge.

Overall 13.9% of patients with uncomplicated pneumonia received guideline similar duration of therapy (Table 3). A greater proportion of HCAP patients (29.0%) received guideline similar therapy duration as compared to CAP patients (6.9%), P<0.01. (Table 3) Median (IQR) duration of therapy was 7 (7,8) days for guideline similar therapy compared to 10 (9,13) days for therapy duration in excess of guideline recommendations. Overall, 97.1 % of patients met clinical stability criteria before day 4 of therapy, yet 50% received ≥4 days of IV therapy [median (IQR) was 4 (3,6) days]. Antimicrobial therapy was generally completed after discharge as only

17.3% received their entire treatment course during hospitalization. Median duration of outpatient PO antimicrobial therapy was twice as long for guideline excessive therapy compared to guideline similar therapy (6 versus 3 days); while duration of inpatient IV and PO antimicrobial therapy were similar. Patients discharged on a fluoroquinolone were more likely to receive guideline similar duration of therapy. The VHA classifies facilities into three levels of complexity with lower scores indicating more complex facilities.[21] Guideline similar therapy duration occurred in 10.4% of cases in lower complexity facilities (level 2 and 3),and 15.1% in more complex facilities (level 1),P=0.01. The median (IQR) duration of therapy was similar for more and less complex facilities, respectively [10 (8,12) versus 10 (8,13) days].

The 28-day post-discharge all-cause-readmission rate for patients who received guideline similar therapy duration was higher (17.4%) than for patients who received therapy duration in excess of guideline recommendations (12.2%), (*P*=0.03). After adjustment for covariates associated with readmission (HCAP, age, prior skilled nursing facility residence, PSI score comorbidity elements), we found no evidence that patients who received guideline similar therapy duration were more likely to be readmitted than were patients who received guideline excessive duration [OR 1.1 (95% CI 0.8,1.7)] (Table 3). Likewise, no difference in 28-day all-cause post-discharge mortality was identified between guideline similar and guideline excessive duration after adjustment for the same covariates [adjusted OR 0.5 (95% CI 0.2, 1.2)] (Table 4).

CDI cases (n=15) were too sparse to adequately perform multivariable logistic regression analysis; however, a higher percentage of patients who received guideline similar duration of

therapy developed CDI compared to patients who received guideline excessive duration of therapy (40.0% versus 13.6%, P<0.01). The median (IQR) duration of therapy for patients that did and did not develop CDI was similar [8 (7, 14) days versus 10 (8,12) days, (p=0.85), respectively]. Patients that developed CDI had a higher rate of HCAP diagnosis (1.5% versus 0.6%; P=0.06), were more likely to have concomitant non-pneumonia infection (40.0% versus 9.5%, P <0.01), have chronic co-morbidity (86.7% versus 59.1%, P=0.03), and to have been admitted to the ICU (26.7% versus 12.1%, P=0.09).

Discussion

IDSA/ATS guidelines for pneumonia duration of therapy generally agree with other professional society guidelines including the British Thoracic Society (BTS) and National Institute for Health and Care Excellence (NICE).[22,23] In contrast to existing evidence and guideline recommendations, this multi-centered evaluation identified prolonged durations of antimicrobial therapy prescribed in 93% and 71% of patients with uncomplicated CAP and HCAP (Table 3), respectively.[3-12] Almost all (97.1%) uncomplicated CAP and HCAP patients met clinical stability criteria before day 4 of hospitalization, yet the median duration of IV therapy was 4 days. Since criteria for IV to PO conversion and the clinical stability definition utilized in this analysis were similar, many patients may have been eligible for PO therapy earlier favorably impacting length of stay, cost, and adverse effects[3,24-27]. Although median (IQR) days of inpatient PO therapy administered was 1(0,3), inpatient observation after PO conversion may not be necessary. The duration of PO therapy was based on calendar days where if a

patient received one dose of a once daily antibiotic (i.e. levofloxacin) they were considered to have received one day of inpatient PO antibiotics even if discharged the same day.

Approximately half of all days of therapy occurred after discharge. While the median therapy duration for inpatients was similar, the median duration of antimicrobials administered upon hospital discharge was twice as long for patients receiving guideline excessive compared to guideline similar duration of therapy. The median excess in antibiotic duration is almost entirely accounted for by excess outpatient days of therapy. This is an important consideration for antimicrobial stewardship programs that tend to focus on inpatient antimicrobial use.

Noteworthy observations include the low rate of respiratory tract culture collection (41%), and frequent use of fluoroquinolones upon discharge. Collection of respiratory tract cultures is recommended for all patients with HCAP and patients with CAP who have risk factors for resistant pathogens—characteristics that were common in this cohort.[3,4] Recently, we identified that respiratory culture collection is associated with increased de-escalation rates in HCAP, and that culture negative patients frequently receive fluoroquinolones.[28] IDSA/ATS CAP guidelines discourage empirically switching to PO fluoroquinolone therapy based on bioavailability considerations alone.[3] Further, fluoroquinolones are considered to be associated with high risk of CDI. [29-30] Prescription of fluoroquinolone upon discharge was associated with guideline similar duration of therapy and was not shown to be associated with CDI; however, power to detect differences between exposures to specific antimicrobials and CDI was low.

CDI was more common in patients with CAP (1.2% vs 0.5%) and HCAP (3.2% vs 0.8%) who received duration of therapy similar with guideline recommendations. This observation is

confounded as patients with CDI had significantly greater comorbidity as well as secondary infections, and tended to more frequently receive ICU care. There were no differences in adjusted rates of readmission or death between patients receiving guideline similar and guideline excessive duration of therapy.

Evaluation strengths included exclusion of patients with complicating conditions possibly requiring prolonged antimicrobial treatment courses, which allowed the evaluation to focus on patients most likely to benefit from shorter course therapy. The definition of appropriate therapy duration was based upon daily assessment of clinical stability criteria that paralleled the CAP guidelines. The definition utilized objective parameters while accounting for patient variability in achieving clinical stability criteria. Finally, the analyses of clinical endpoints suggest that shorter duration of therapy may be as safe and effective as longer duration of therapy in uncomplicated pneumonia.

Limitations include those common to other analyses conducted within the VHA, including a predominantly elderly male cohort.[31] Only ICD-9CM codes consistent with a discharge diagnosis of pneumonia were used to identify the cohort, and clinical impressions not documented in the medical record may have impacted clinician's treatment duration decisions. The upper limit of appropriate duration of therapy for CAP was arbitrarily set at up to 3 days beyond meeting clinical stability criteria to provide a "reasonable" duration of appropriate therapy beyond clinical stability to in order to operationalize the duration of therapy recommendations within the context of the IDSA/ATS guidelines. Additionally, confidence intervals for the odds ratios of readmission and mortality were broad and thus too imprecise to

determine whether guideline similar durations increased or decreased readmission or mortality in comparison with therapy that exceeded guideline recommendations. We could not fully assess the potential for association between guideline excessive therapy duration and risk for CDI due to sparse cases. Finally, non-VA prescription data were not available for all patients, and we relied on intended duration of therapy as recommended by the discharging provider in 4.1% of cases.

Most quality assessments of pneumonia treatment have focused on antimicrobial selection and timely administration or conversion from IV to PO therapy.[32,33] This evaluation identified potential opportunities for expansion of antimicrobial stewardship activities during the transition of care setting. The efficacy of short-course β-lactam, macrolide, or fluoroquinolone therapy for CAP appears equivalent to longer treatment regimens with no difference in adverse event rates suggesting that optimal duration of therapy may be a rational target for quality improvement.[5-12,15,32] Recommendations for HCAP duration of therapy are extrapolated from a prospective multi-centered study which randomized patients with Hospital Acquired Pneumonia to receive 8 versus 15 days of therapy that identified similar outcomes to ours.[4,12]

Single-center studies have identified that antimicrobial therapy for pneumonia is frequently prescribed for longer than recommended by guidelines, which found a similar median duration of therapy as our evaluation.[15,16] Similar to Jenkins et al., we observed a high rate of fluoroquinolone prescriptions upon discharge.[16]

There are few published examples of interventions designed to limit excessive duration of therapy, particularly for antimicrobials prescribed upon hospital discharge.[15,34,35] Serial procalcitonin measurements have been used to guide duration of therapy for pneumonia; however, the cost-benefit ratio of procalcitonin measurement is unclear.[36,37] Procalcitonin use was uncommon and none of the participating facilities in our evaluation utilized a specific algorithm to guide therapy duration. Limited data suggests that patient-level prospective audit with feedback may be effective. Advic et al. evaluated management of presumed CAP before and after education and prospective feedback to medical teams concerning antimicrobial selection and duration of therapy.[15] The intervention led to a decrease in median (IQR) duration of therapy from 10 (8-13) to 7 (7-8) days without increasing clinical failure or readmission rates. We recently reported a single center evaluation in which pharmacists utilizing a decision support tool while performing discharge medication reconciliation were able to reduce excessive mean duration of therapy from 9.5 (± 2.4) days to 8.3 (± 2.9) days in patients without complicated pneumonia; with a 19.2% reduction in duration of therapy prescribed at discharge (Caplinger C, et al. Am J Health Syst Pharm. Accepted April 2016. In press).[38] A similar approach utilizing pharmacists performing discharge review has recently been reported in a community hospital.[39]

Future work should recognize that few patients complete their entire course of therapy as inpatients, and the majority of treatment is prescribed upon discharge. Pivotal time-points for antimicrobial stewardship intervention include day 2-3 of hospitalization when conveying suggestions for antimicrobial de-escalation and/or IV to PO conversion, and towards the end of hospitalization during discharge planning. While it may not be feasible for antimicrobial

stewards to review all uncomplicated cases of pneumonia during hospitalization, most facilities have a systematic process for reviewing medications during transitions of care. We believe that interventions intended to assess and recommend shortened courses of therapy are appropriate. These interventions should include a mechanism for support by stewardship personnel or other Infectious Diseases specialists. Based on our evaluation, the ASTF produced and disseminated Clinical Guidance documents and tools to triage pneumonia case severity and assess response to therapy. Qualified personnel are encouraged to use this information to make recommendations to providers regarding excessive duration of therapy for uncomplicated cases where appropriate. Other work should include an in depth assessment of clinical outcomes related to treatment duration, investigation of provider rationale for prolonged treatment, and duration of antimicrobial therapy prescribed upon discharge for other common disease states. Finally, manual chart review to classify uncomplicated cases and related outcomes was laborious and automated case identification is technologically plausible and should be explored.[40]

In conclusion, this National VHA MUE found that patients with uncomplicated pneumonia were commonly prescribed antimicrobials for duration of therapy in excess of guideline recommendations. Patients with uncomplicated pneumonia who received therapy duration consistent with guideline recommendations did not have significantly different all-cause readmission and death rates compared to patients receiving prolonged treatment. Approximately half of all therapy was prescribed upon hospital discharge, and clinicians as well as antimicrobial stewardship programs should consider these findings to address excessive duration of antimicrobial therapy upon hospital discharge.

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Table 1. Demographic and other Characteristics of the Pneumonia Cohort (n=1739)

Characteristic	
Age (y), Mean (± S.D.)	71.8(12.7)
Gender (Male) [n, (%)]	1680(96.6)
Living environment at time of index admission [n, (%)]	
Home	1416 (81.4)
VA Community-based Living Center	88(5.1)
Non-VA long-term skilled care facility	95(5.5)
Assisted Living Facility	52 (2.9)
Not documented	46 (2.7)
Other	29(1.7)
Prior healthcare exposures [n, (%)]	
Prior hospitalization within last 90 d	310(17.8)
Residence in a long term skilled care facility in last 90d	209(12.0)
Chronic dialysis within last 28 d	52(3.0)
Intravenous antimicrobials within last 28 d	76(4.4)
Wound, tracheostomy, or ventilator care in last 28 d	37(2.1)
Community-Acquired Pneumonia	1195 (68.7)
Healthcare-Associated Pneumonia	544(31.3)
Comorbidities [n, (%)]	
Renal disease	438(25.2)
Liver disease	39(2.2)
Congestive Heart Failure	436(25.1)
Cerebrovascular disease	356(20.4)
Neoplastic disease (excluding skin)	384(22.1)
Severity of Illness [n, (%)]	
Pneumonia Severity Index	
Class I	30(1.8)
Class II	198(11.4)
Class III	349(20.1)
Class IV	759(43.6)
Class V	403 (23.2)
Intensive Care Upon Admission	212(12.2)
Culture collection ≤ 48 hours of admission [n, (%)]	1687 (97.0)
Blood	1631(96.7)
Lower respiratory tract (sputum)	673(39.9)
Bronchoalveolar lavage	20(1.2)
Urine	632(37.5)
Skin/wound	3(0.2)
Other	158(9.4)
Facility Complexity [n, (%)]	
Level 1a-c	1286(74.0)
Level 2	437(25.1)
Level 3	16(0.9)

Table 2. Antimicrobials Administered During Hospitalization and Dispensed Upon Discharge

Inpatient Antimicrobials Administered*				
	Portion of Cohort Receiving Antimicrobial n=1739	**Therapy Duration Similar w/Guidelines[n,(%)] n=241**	**Therapy Duration Exceeding Guidelines [n,(%)] n=1498**	**Significance**
3rd gen. Cephalosporins	809 (46.5)	75(31.1)	734(49.0)	<0.001[a]
Fluoroquinolones	836(48.1)	114(47.3)	722(48.2)	0.80
Macrolides	788(45.3)	90(37.3)	698(46.6)	<0.01[a]
Pseudomonal β -lactams	692(39.8)	138(57.3)	554(37.0)	0.01[b]
Anti-MRSA antimicrobials	663(38.1)	135(56.0)	528(35.3)	<0.01[b]
Other β-lactams	139(8.0)	10(4.2)	129(8.6)	0.02
Tetracyclines	119(6.8)	14(5.8)	105(7.0)	0.49
Other	97 (5.6)	15(6.2)	82(5.5)	0.64
Antimicrobials Dispensed or Recommended at Discharge†				
	Portion of Cohort Receiving Antimicrobial n=1471	**Therapy Duration Similar w/Guidelines [n,(%)] n=151**	**Therapy Duration Exceeding Guidelines [n,(%)] n=1320**	**Significance**
3rd gen. Cephalosporins	285 (19.4)	27(17.9)	258(19.6)	0.62
Fluoroquinolones	813(55.3)	95(62.9)	718(54.4)	0.05
Macrolides	203(13.8)	20(13.3)	183(13.9)	0.83
Pseudomonal β -lactams	31(2.1)	4(2.7)	27(2.1)	0.62
Anti-MRSA antimicrobials	45(3.1)	6(4.0)	39(3.0)	0.49
Other β-lactams	239(16.3)	13(8.6)	226(17.1)	0.01
Tetracyclines	95(6.5)	10(6.6)	85(6.4)	0.93
Other	44 (3.0)	5(3.3)	39(3.0)	0.81

Legend: *: Includes all patients (n=1739) administered at least one dose of antimicrobial. †: Includes all patients who had a VA prescription dispensed within 24 hours of hospital discharge or had an antimicrobial and duration recommended in the Discharge Summary. **3rd gen. Cephalosporins:** ceftriaxone, cefotaxime, cefpodoxime, cefprozil, cefdinir, cefuroxime. **Fluoroquinolones:** moxifloxacin, levofloxacin, ciprofloxacin. **Macrolides:** azithromycin, clarithromycin. **Pseudomonal β –lactams:** piperacillin/taz., cefepime, ceftazidime, aztreonam, meropenem, imipenem. **Anti-MRSA antimicrobials:** vancomycin, linezolid, ceeftaroline. **Other β-lactams:** ampicillin/sulb., amoxicillin/clav. ampicillin, amoxicillin, penicillin, nafcillin, dicloxacillin, cefazolin, cephalexin, ertapenem. **Tetracyclines:** doxycycline, minocycline, tigecycline. **Other:** clindamycin, metronidazole, trimethoprim/sulfa., gentamicin, tobramycin, amikacin, polymyxcin B.

[a] Note: The majority of patients in this group were CAP patients for whom the guideline similar duration of therapy was less than that allowed for HCAP patients

[b] Note: The majority of patients in this group were HCAP patients for whom the guideline similar duration of therapy was shorter than that allowed for CAP patients

Table 3. Duration of Antimicrobial Therapy Administered for Uncomplicated Pneumonia and Clinical Outcomes of Interest

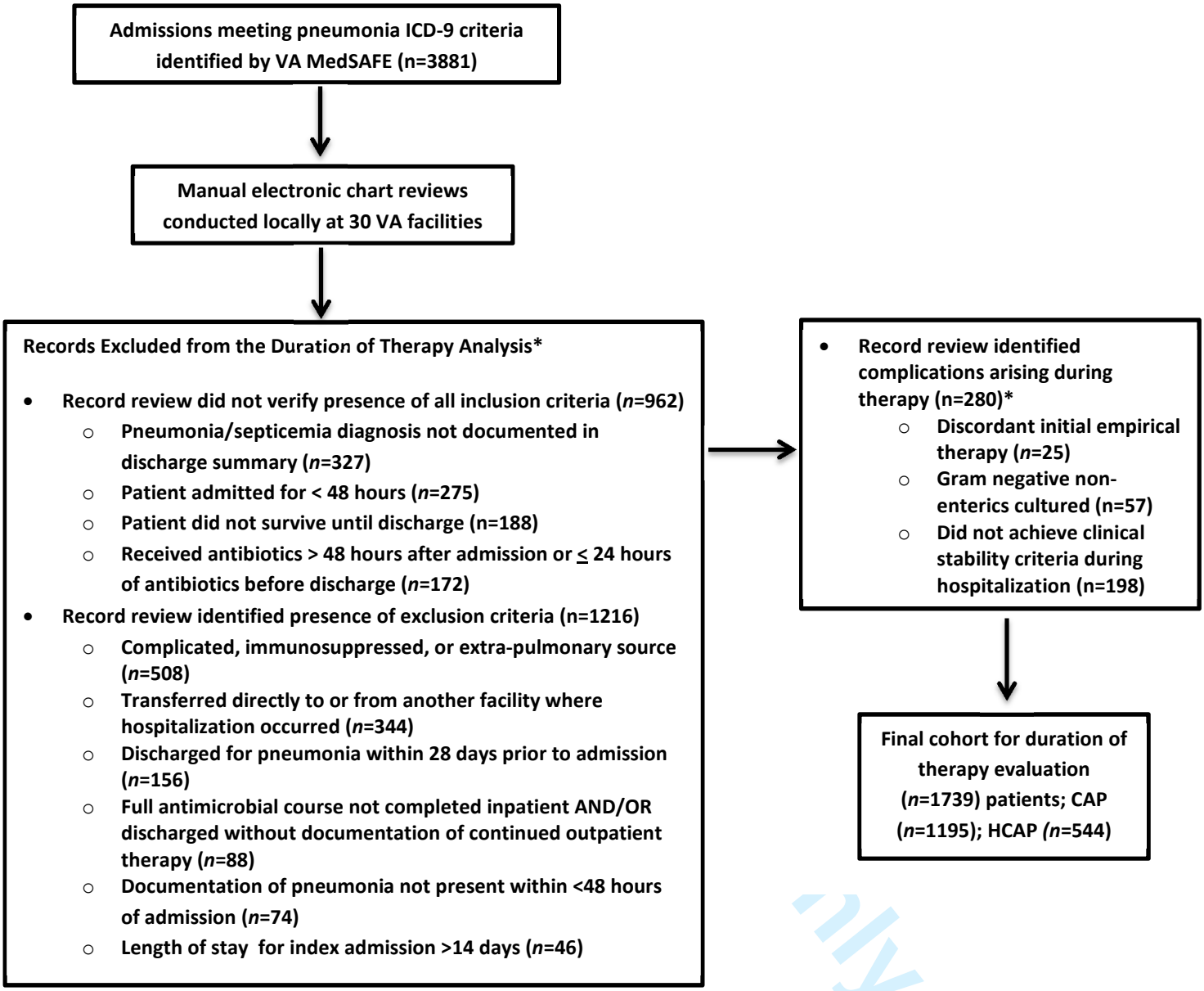
Outcome	Therapy Duration Similar w/IDSA/ATS Guidelines	Therapy Duration in Excess of IDSA/ATS Guideline Recommendations	Significance
Antimicrobial duration consistent with guideline recommendations [n,(%)]	241(13.9)	1498(86.1)	NR
CAP[1,2]	83(6.9)	1112(93.1)	NR
HCAP[1,2]	158(29.0)	386(71.0)	NR
Total days of therapy for pneumonia [Median, (IQR)]	7(7,8)	10(9,13)	NR
CAP	6(5,9)	10(8,12)	<0.01
HCAP	7(7,8)	11(10,14)	<0.01
Days of IV therapy administered for pneumonia [Median, (IQR)]	4(3,7)	4(3,6)	0.50
Days of PO inpatient therapy administered [Median, (IQR)]	1(0,3)	1(0,3)	0.78
Days of PO outpatient therapy dispensed at discharge [Median, (IQR)] [3]	3(2,5)	6(4,7)	<0.01
Days of PO outpatient therapy recommended in Discharge Summary for patients without a VA prescription [Median, (IQR)][4]	3(2,4)	5(4,7)	<0.01
Aggregate 28-day hospital readmission [n,(%)]	42(17.4)	183(12.2)	0.03
CAP [n,(%)][5-7]	7(8.4)	112(10.1)	0.58
HCAP [n,(%)][5-7]	35(22.2)	71 (18.4)	0.28
Aggregate 28-day CDI rate [n,(%)]	6(2.5)	9(0.6)	0.03
CAP [n,(%)][5,8]	1(1.2)	6(0.5)	0.44
HCAP [n,(%)][5,8]	5(3.2)	3(0.8)	0.04
Aggregate 28-day death after discharge [n,(%)]	6 (2.5)	52 (3.5)	0.43
CAP [n,(%)][8,5]	1(1.2)	33(3.0)	0.35
HCAP [n,(%)][5,8]	5(3.2)	19(4.9)	0.37

Legend:
[1] Denominators for each row are stratified by all included and non-excluded patients who had CAP and HCAP, respectively
[2] CAP vs HCAP $p<0.01$
[3] $n=1403$
[4] $n=76$
[5] Denominators for each row are stratified by guideline concordance and discordance and patients who had CAP and HCAP, respectively
[6] 28-day hospital readmission, guideline concordant therapy, CAP vs HCAP $p<0.01$
[7] 28-day hospital readmission, guideline discordant therapy, CAP vs HCAP $p<0.01$
[8] HCAP vs CAP p values not significant
NR=Not Relevant

Table 4. Multivariable Models for 28-Day Readmission and Mortality.

Model Variables	Odds Ratio	±95% Confidence Interval	*P* value
Readmission Model			
Duration of antibiotics	1.11	(0.75, 1.64)	0.62
HCAP	1.94	(1.38, 2.72)	<0.01
Age	1.01	(1.00, 1.03)	0.04
Prior skilled nursing facility residence	0.91	(0.59, 1.40)	0.67
PSI score comorbidity elements	-	-	-
Neoplastic disease	1.20	(0.86, 1.67)	0.29
Liver disease	1.55	(0.66, 3.64)	0.31
CHF	1.15	(0.83, 1.59)	0.41
Cerebrovascular disease	1.06	(0.75, 1.50)	0.75
Renal disease	1.51	(1.09, 2.08)	0.01
Mortality Model			
Duration of antibiotics	0.53	(0.23, 1.22)	0.14
HCAP	2.53	(1.38, 4.65)	<0.01
Age	1.06	(1.03, 1.09)	<0.01
Prior skilled nursing facility residence	0.79	(0.38, 1.66)	0.53
PSI score comorbidity elements	-	-	-
Neoplastic disease	1.03	(0.57, 1.87)	0.91
Liver disease	<0.001	(<0.001, >999.9)	0.98
CHF	0.73	(0.39, 1.38)	0.34
Cerebrovascular disease	0.82	(0.43, 1.56)	0.55
Renal disease	0.72	(0.39, 1.35)	0.31

Figure 1. Application of Inclusion and Exclusion Criteria for the Pneumonia Duration of Therapy Evaluation.



* Patients may have met more than one criteria resulting in exclusion.