A Statewide Collaborative Quality Initiative to Improve Antibiotic Duration and Outcomes of Patients Hospitalized with Community-Acquired Pneumonia

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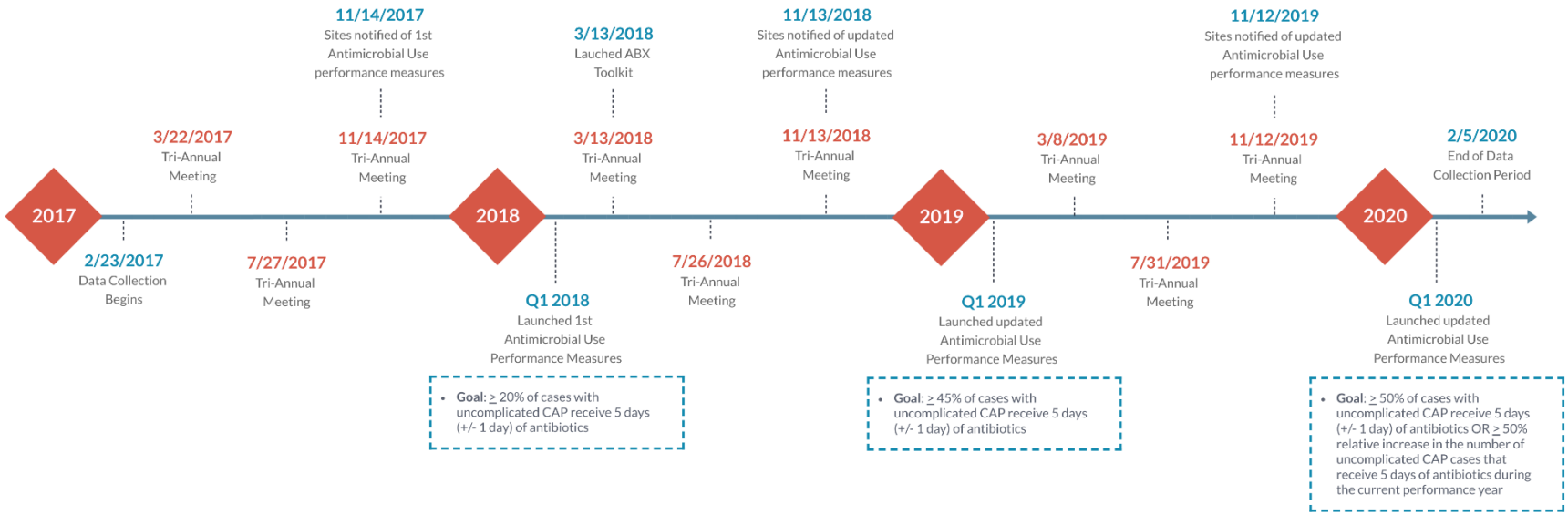
Supplementary Appendix

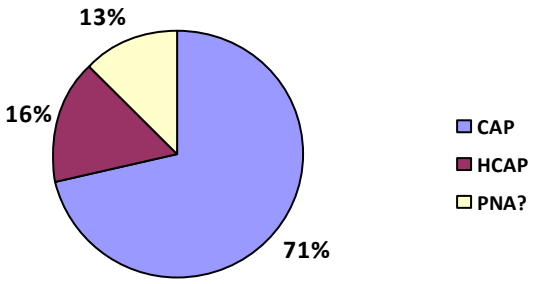
eFigure 1. Timeline of Michigan Hospital Medicine Safety Consortium Events



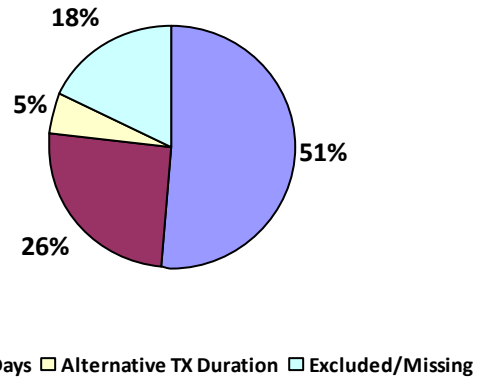
HMS - Antimicrobial Use Report

Data has been modified to protect hospital confidentiality

Pneumonia Distribution[1,8]
Total: 50000

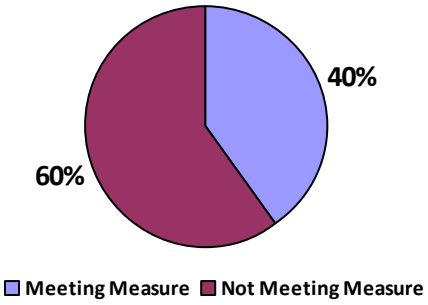


CAP: Expected duration based on clinical criteria [2,3]



Median duration for cases receiving excess duration: 13

CAP 5 Day Performance Metric[3,4,5,6,7]



Cases not meeting CAP 5 day performance metric: Patient ID numbers

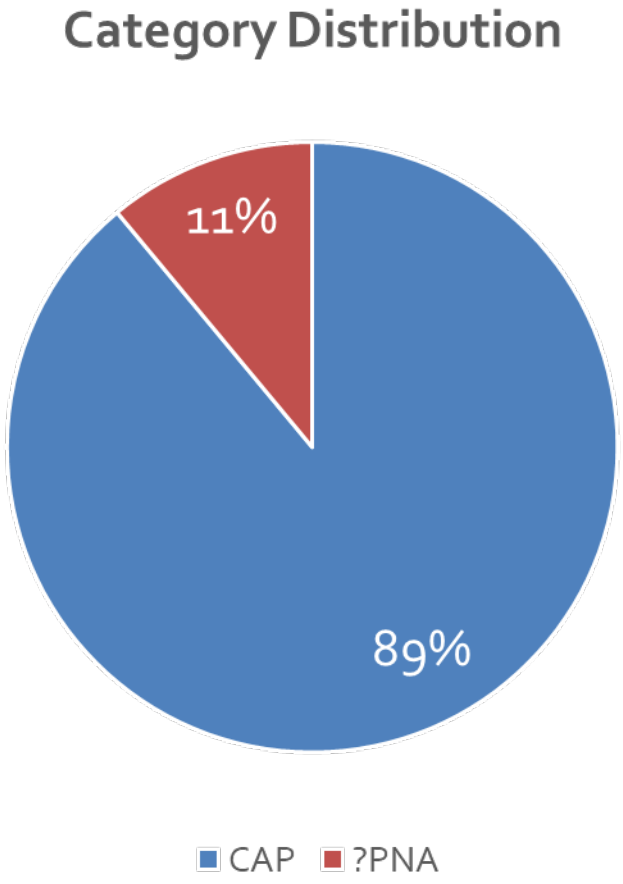
Top 3 Antibiotics for CAP cases

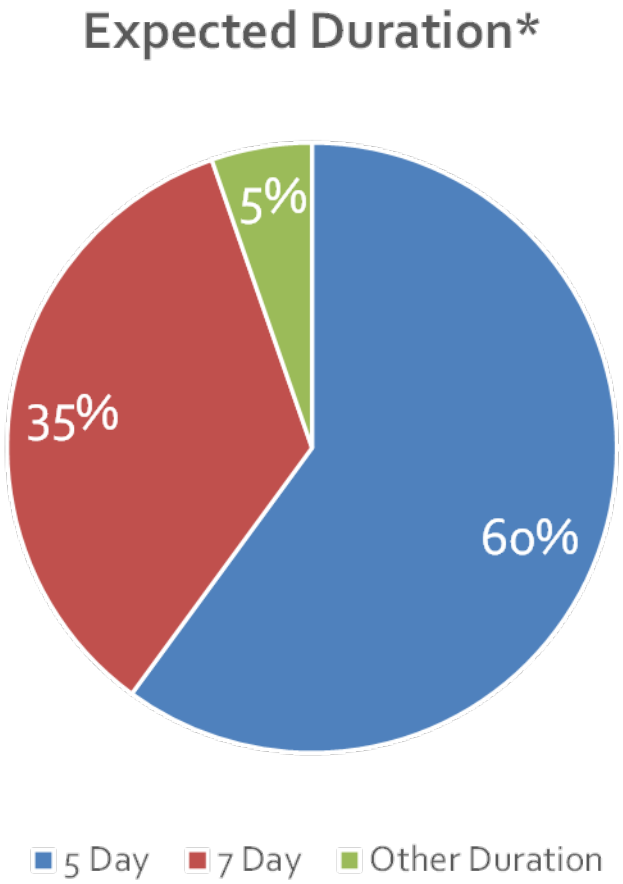
Inpatient ABX x% (n)	Discharge ABX x% (n)
1. Ceftriaxone 60% (20000)	1. Levofloxacin 30% (5000)
2. Azithromycin 70% (45000)	2. Azithromycin 35% (5500)
3. Vancomycin 33% (6000)	3. Augmentin 15% (2000)

Footnotes:

1. To meet the definition of pneumonia, a case must have radiographic evidence and 2 or more signs or symptoms of pneumonia.
2. Treatment durations 1 day more than the expected duration were also considered appropriate.
3. Patients Excluded: Those who have any of the following: Legionella, Pulmonary complication (i.e empyema/parapneumonic effusion, cavitation, loculations), Pulmonary procedure (i.e. VATS)Bacteremia (including pneumococcal; excluding contaminants), PCP Pneumonia, congenital/acquired immunodeficiency, died or transferred during hospitalization, Missing critical data to calculate duration.
4. Based of factors of clinical stability and case factors.
5. Cases treated >/= 2 days shorter than expected duration are not included.
6. Treatment durations 1 day more than the expected duration were also considered appropriate.
7. Effective duration is defined as the total duration of antibiotic treatment with the exception that antibiotic days that cultures revealed resistance to the antibiotic are not counted for the day of culture collection and 3 days after.
8. Beginning in 2021, HMS modified to use the updated (2019) ATS guidelines for diagnosis and treatment of pneumonia.

Pneumonia Categories and Expected Pneumonia Duration Breakdown



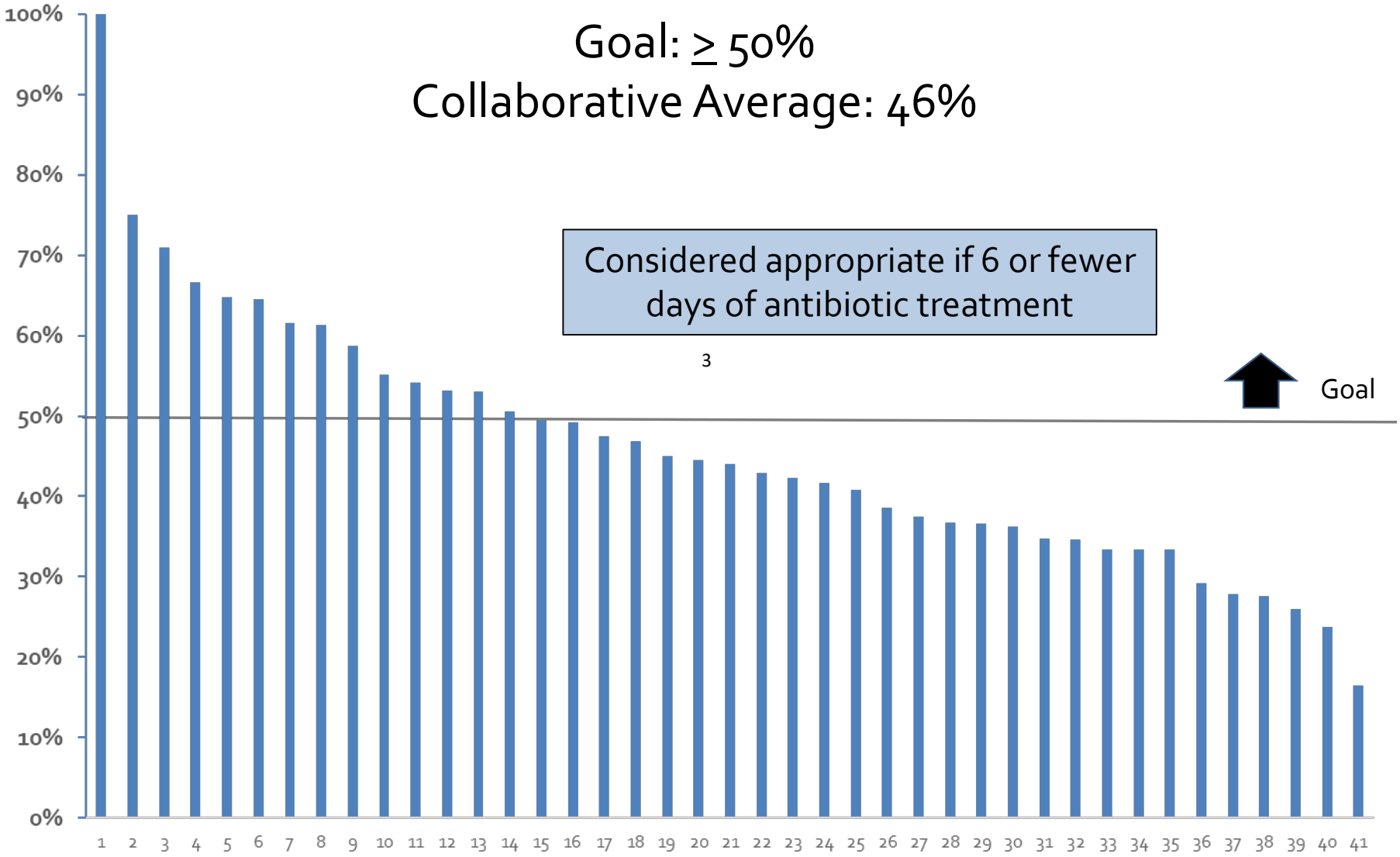


?PNA is patients not meeting criteria for pneumonia

*excluding ?PNA

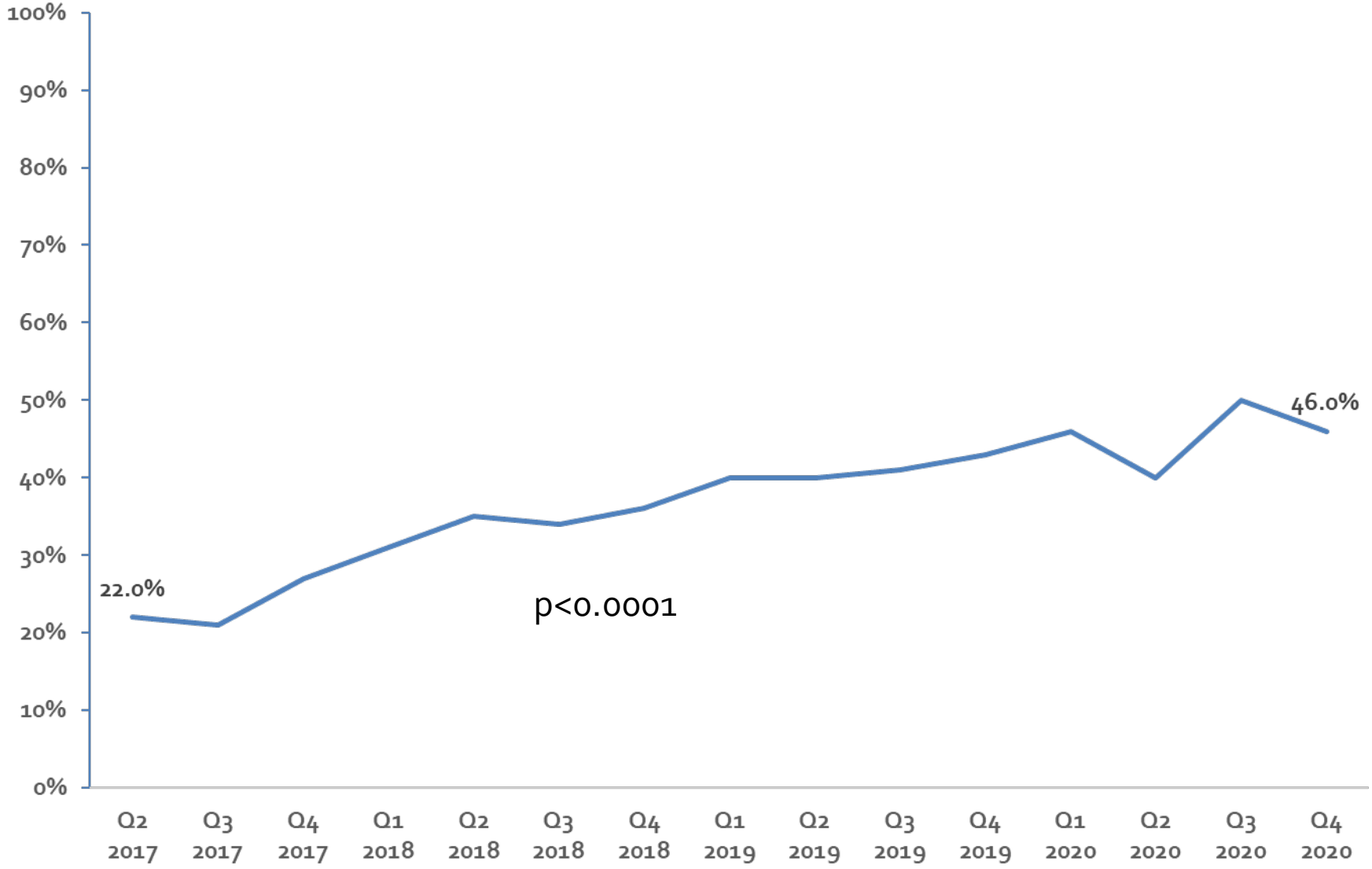
*Data have been modified to protect hospital confidentiality

CAP 5 Day: % Treated with 5 Days of Antibiotics by Hospital (Q4)



*Data have been modified to protect hospital confidentiality

CAP 5 Day: % of Patients Treated with 5 Days of Antibiotics by Quarter*



*Data have been modified to protect hospital confidentiality

HMS ANTIMICROBIAL INITIATIVE TIER 1 TOOLKIT: QUICK REFERENCE GUIDE

This reference document provides a summary of the Tier 1 Toolkit for the HMS Antimicrobial Initiative that aims to implement global strategies to improve antimicrobial use

Convene a Workgroup to Focus on Tier 1 Strategies

The workgroup will likely be a new subgroup of your antimicrobial stewardship team. For maximum impact, the workgroup should consist of a multidisciplinary team that includes (but is not limited to) key stakeholders, such as a hospitalist, infectious disease physician and/or pharmacist, emergency medicine physician, house officers, IT personnel, microbiology lab representative, and nursing.

Tools and Resources:

- HMS site reports (hard copy distributed at collaborative wide meetings and live reports available daily via the HMS data entry system)
- CDC Core Elements of Hospital Antibiotic Stewardship Programs

Develop and Share Institutional Guidelines for Community-Acquired Pneumonia (CAP)

Develop institutional guidelines, locally-adapted from national and HMS guidelines, for treatment of community-acquired pneumonia (CAP). If institution specific guidelines already exist, they should comply with the following:

CAP

Institutional guidelines should:

- Recommend 5-day antibiotic treatment duration for uncomplicated CAP
- Review the risk factors for Multi-Drug Resistant Organisms (MDRO) and/or Healthcare-Associated Pneumonia (HCAP)
- Provide recommendations for transition to oral therapy
- De-emphasize fluoroquinolones

Tools and Resources:

- IDSA, HMS, and Institutional Guidelines:
  - CAP
- HMS Pocket Card Examples:
  - CAP

Integrate and Operationalize Institutional Guidelines for CAP

Integrate recommendations into key processes within the healthcare system such as into order sets, individual orders, discharge planning/processes, required yearly education for staff, etc.

Educate providers, including hospitalists, internal medicine, family medicine, emergency medicine physicians, residents, advanced practice professionals (APPs), and nursing staff about antibiotic resistance and appropriate antimicrobial prescribing.

Educate patients and families about antibiotic resistance and appropriate antimicrobial prescribing.

After 3 months of guideline use, obtain provider feedback from multiple groups (including hospitalists, internal medicine, emergency department, etc.), and modify accordingly.

Tools and Resources:

- CAP Order Set Example
- Patient Education Handout Example
  - Patients: *What you need to know when you are prescribed an antibiotic*

Interventions continued on back page

Michigan Hospital Medicine Safety Consortium Antibiotic Use Toolkit Continued
(only pieces relevant for CAP treatment are shown)

Reduce Duration of Antibiotic Treatment for Uncomplicated CAP to 5 Days

Educate providers on the justification for 5 days of therapy for uncomplicated CAP

Evaluate and understand differences in provider groups (e.g., hospitalists, emergency medicine physicians). Target interventions to specific provider groups as necessary.

Encourage documentation of dose, indication and duration in the progress notes and on discharge.

Focus efforts on discharge prescribing, as HMS data shows that discharge prescriptions account for 80% of inappropriate antibiotic treatment for uncomplicated CAP.

Tools and Resources:

- Example of Email Feedback on Provider Performance for Duration of CAP Treatment
- Factsheet Emphasizing Focus on Discharge Prescriptions
- 72-hour Antibiotic Time Out Checklist
- Example of Hospital Newsletter Incorporating HMS Data
- CAP Pocket Card

De-escalate Antibiotic Treatment for Pneumonia

Utilize 72-hour Antibiotic Time Outs after starting antibiotics, including:

- Assess indication(s) for antibiotics
- Review culture results
- Adjust drug selection (de-escalate) and doses
- Consider switching to oral route
- Decide and document treatment duration

Encourage de-escalation of vancomycin for pneumonia with negative respiratory cultures and/or nasal swabs for MRSA.

Utilize HMS data to provide audit and feedback directly to providers regarding:

- Coverage of methicillin-resistant *Staphylococcus aureus* (MRSA) with negative MRSA nasal swabs and/or respiratory cultures
- Coverage of *Pseudomonas* with negative respiratory cultures

Utilize pharmacists to review cultures, and if positive, ensure that the narrowest, appropriate antibiotic coverage is chosen for the diagnosis.

Tools and Resources:

- Examples from Intermountain Health for Pharmacist-Driven Tools to Aid in De-escalation
- 72-hour Antibiotic Time Out Checklist
- HMS Site Reports (hard copy distributed at collaborative wide meetings and live reports available daily via the HMS data entry system)

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Michigan Hospital Medicine Safety Consortium Antibiotic Use Toolkit Literature and Resources Summary
(only pieces relevant for CAP treatment are shown)

Reduce Duration of Antibiotic Treatment for Uncomplicated CAP to 5 Days	• Educate providers on the justification for 5 days of therapy for uncomplicated CAP • Review CAP cases identified by HMS to implement high-yield interventions for recurrent problems • Evaluate and understand differences in provider groups (e.g., hospitalists, emergency medicine providers). Target interventions to specific provider groups as necessary. • Evaluate existing order sets to ensure antibiotic preferred options, doses, and durations are consistent with institutional pneumonia guidelines. • Require documentation of dose and indication of antibiotics prescribed in the antibiotic order. • Encourage documentation of dose, indication, and duration of antibiotics in the progress note. • Require a 72-hour Antibiotic Time Out, during which total duration should be discussed. • Focus efforts on discharge prescribing, as HMS data shows that discharge prescriptions account for 80% of inappropriate antibiotic treatment for uncomplicated CAP. • Require documentation of the total duration of antibiotics in the discharge summary, potentially incorporating an area for antibiotic duration to be filled out in an automated discharge process. • Incorporate nursing and pharmacy into review of the discharge antibiotic. • Provide audit and feedback directly to providers regarding the duration of antibiotics they use for patients with uncomplicated CAP. • Consider incorporating compliance with treatment duration for uncomplicated CAP as part of hospitalists' performance targets (for compensation).	**Resources & Tools:** • HMS Document: Treatment duration for uncomplicated community-acquired pneumonia: the evidence in support of 5 days. • Review HMS site reports (hard copy distributed at collaborative wide meetings and live reports available daily via the HMS data entry system) for the following: ▪ Uncomplicated CAP treated with 5 days of antibiotics ▪ Types of Reports Available via HMS Registry: Hospital Specific, Provider Group Specific (i.e. hospitalist v. emergency room physician), or Provider Specific • HMS Guideline: ▪ CAP • CAP Pocket Card (Appendix C) ▪ Consider modifying to poster size for posting in workrooms • Factsheet Emphasizing Focus on Discharge Prescriptions (Appendix I) • Educational Videos: ▪ Vaughn V. Antibiotic Stewardship: Community-Acquired Pneumonia: for Providers • 72-hour Antibiotic Time Out Checklist (Appendix J) • Example of hospital newsletter incorporating HMS data (Appendix K) • Example of email feedback on provider performance for duration of CAP treatment (Appendix L) **References:** • Avdic E et al. Impact of an Antimicrobial Stewardship Intervention on Shortening the Duration of Therapy for Community-acquired Pneumonia. *Clin Infect Dis* 2012. ▪ Reduced treatment duration of CAP with educational lectures based on survey results, and post-prescription pharmacy review with verbal feedback • Yogo N et al. Intervention to Reduce Broad-Spectrum Antibiotics and Treatment Durations Prescribed at the Time of Hospital Discharge: A Novel Stewardship Approach. *Infect Contol Hosp Epidemiol 2014* ▪ Reduced antibiotic duration prescribed at discharge by developing a guideline for antibiotic selection and

Michigan Hospital Medicine Safety Consortium Antibiotic Use Toolkit Literature and Resources Summary Continued (only pieces relevant for CAP treatment are shown)

		treatment duration and performing pharmacy audit and feedback of discharge prescriptions • Foolad F et al. A multicenter stewardship initiative to decrease excessive duration of antibiotic therapy for the treatment of community acquired pneumonia. *J Antimicrob Chemother* 2018 ▪ Treatment duration for CAP was reduced by updating institutional CAP guidelines, providing educational sessions, and performing daily audit and feedback on appropriate treatment duration for CAP patients

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D.I.S.Ch.A.R.G.E. Antibiotics: FACTS AND SOLUTIONS

D.I.S.Ch.A.R.G.E. Antibiotics: FACTS AND SOLUTIONS

D.I.S.Ch.A.R.G.E!

How to improve antibiotic prescribing at hospital discharge.

Defaults and order sets

- Consider use of default durations, default transitions from IV to oral, and recommendations within computerized order-entry to improve early transition to appropriate oral therapy (which can then be continued on discharge)
- Make sure default orders and order sets recommend guideline-appropriate antibiotic choice and duration

Incentivize

- Consider incorporating discharge antibiotic metrics into quality or compensation targets

Discharge **S**ummary

- Require documentation of total antibiotic duration in discharge summary
  - Consider enforcing this rule by using smart phrases with hard stops for antibiotic duration in the discharge summary
  - E.g.: To treat (disease), Mr(s) X will continue (abx name) for X additional days, for X days total.

Checklist

- Use an antibiotic checklist at discharge to evaluate and ensure antibiotic appropriateness

Audit and Feedback

- Audit and provide feedback of discharge prescriptions (e.g., pharmacists or stewardship team, performance review, quality compensation targets)

Review: Incorporate antibiotic appropriateness into discharge review process using different members of the care team

- For example
  - With pharmacists (when reviewing or filling discharge medications)
  - With bedside nurse (when reviewing discharge medications)
  - During multidisciplinary/discharge rounds

Guidelines

- Make sure your institutional guidelines include oral antibiotic recommendations for discharge for common infections (e.g., pneumonia, urinary tract infection)
  - Prioritize non-fluoroquinolone antibiotics in guidelines
  - Recommend alternatives to fluoroquinolone antibiotics when possible
  - Provide a recommendation for appropriate duration for different disease states (e.g., 5 days for community-acquired pneumonia), making sure that total duration includes effective inpatient therapy

Educate providers on guidelines and discharge recommendations

- Formal lectures to residents, physicians (e.g., hospitalist, ID, ED), APPs
- Consider using pocket card
- Consider the use of multiple ways to post guidelines (e.g., websites, apps, printed books)

ANTIBIOTIC TIME-OUT ✓ CHECKLIST

How to use this checklist:

- Review the need for antibiotics on each patient on antibiotics daily. This review allows you to evaluate new information, such as clinical improvement and new culture results, to update your treatment plan. At a minimum, there are two key times to review antibiotic treatment:

  - ✓ 48-72 hours after admission
    - A lot of diagnostic information has likely returned by now and the patient has likely either improved (or deteriorated) on current therapy. It's therefore time to reassess all information

  - ✓ At hospital discharge
    - Patients being discharged are often less sick and recovering, but not completely better. Sometimes they need to continue antibiotics to treat the infection for which they were hospitalized. This is a great time to make sure the rest of their treatment is guidelines appropriate

  - ✓ Other useful times include: any transition of care, change in status, or handoff between providers.

ANTIBIOTIC TIME-OUT CHECKLIST

Do we still think this patient has a bacterial infection or is another diagnosis more likely?

- Problems which initially begin as symptoms (e.g., dyspnea) should be updated to diagnoses (e.g., community-acquired pneumonia, acute on chronic systolic heart failure).
- Is the diagnosis still infectious? Bacterial, fungal, viral?
- If the problem is no longer thought to be due to an infection, stop antibiotics.

If the patient has a bacterial infection, can we de-escalate?

- If culture results have returned, de-escalate to the narrowest effective antibiotic.
- If culture results are negative, the patient is improving, and the patient was on broad-spectrum antibiotics, de-escalate by removing anti-MRSA and anti-pseudomonal coverage.
  - This does not need to be done over multiple days but can be done at the same time (e.g., changing vancomycin + zosyn to ceftriaxone)
- If no cultures were obtained, but the patient is improving, consider de-escalation.

Can the patient be switched to an oral antibiotic?

- If a patient has a functional GI tract, is tolerating oral intake, and is hemodynamically stable then usually an oral antibiotic is appropriate.
  - Exceptions include complicated infections (e.g., meningitis, endocarditis, bacteremia)
- A patient on oral antibiotics is often able to be discharged.

How long should the patient receive antibiotics?

- In order to prevent patients from staying on prolonged courses, plan a course early.
- Patients should receive the minimum effective antibiotic duration for their diagnosis.
  - For example, patients with community-acquired pneumonia who are improving, afebrile, and clinically stable by day 2 or 3 only need 5 *total* days of antibiotics, including any effective IV therapy they receive.

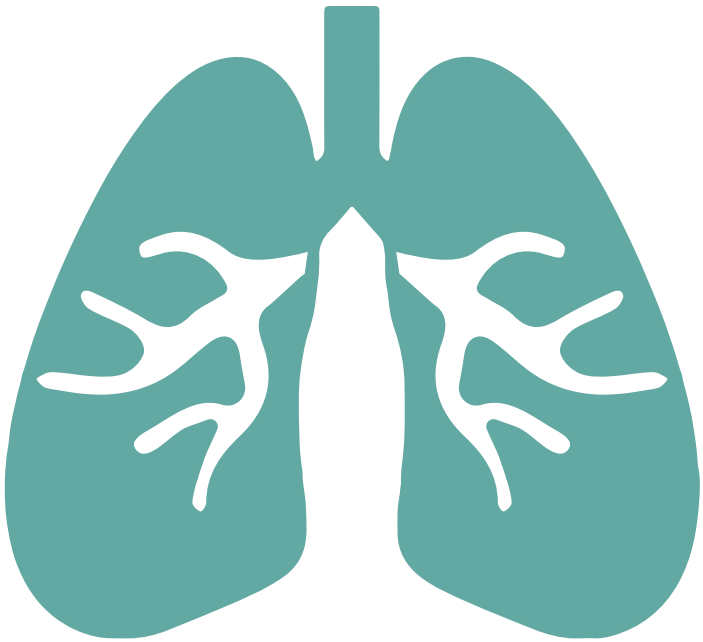
Now that you have decided on a final antibiotic, is it prescribed at the right dose?

- Make sure you consider the type of infection, route of administration, renal and hepatic function, and interaction(s) with other medications.

Have we documented dose, duration and indication for all antibiotics?

- In the discharge summary, you should also include total planned antibiotic duration (Including start and planned stop dates).

Treatment Duration for Uncomplicated Community-Acquired Pneumonia: The Evidence in Support of 5 Days



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Executive Summary

National consensus guidelines created jointly by the Infectious Diseases Society of America (IDSA) and the American Thoracic Society (ATS) recommend 5 days of antibiotic therapy for adult patients with community-acquired pneumonia (CAP) who have been afebrile for 48 hours and have no more than 1 CAP-associated sign of clinical instability.

Patients with uncomplicated CAP treated at many hospitals, including hospitals participating in the Michigan Hospital Medicine Safety Consortium (HMS), continue to get longer treatment durations without evidence to support that these longer durations lead to better outcomes. The 5-day treatment duration is directly or indirectly supported by the following:

- Five (5) randomized controlled trials, plus an additional sub-group analysis, which demonstrate no significant difference in key outcomes for short versus extended-course antibiotics including clinical improvement, bacteriological improvement, radiographic resolution, adverse effects, mortality, recurrence, and length of hospital stay.
- Three (3) quasi-experimental studies, plus a follow-up study, which demonstrate no significant difference in key outcomes for short versus extended-course antibiotics including treatment failure, recurrence, mortality, length of hospital stay, and re-admission.
- Two (2) systematic reviews with meta-analyses, based on 20 randomized controlled trials collectively, which demonstrate no significant difference in effectiveness and safety of short versus extended-course antibiotic therapy including clinical failure, mortality, and bacterial eradication.

A detailed, annotated list of key references in support of 5-day antibiotic treatment duration for uncomplicated CAP patients follows.

1. Haas MK, Dalton K, Knepper BC et al. Effects of a Syndrome Specific Antibiotic Stewardship Intervention for Inpatient Community Acquired Pneumonia. Open Forum Infect Dis. 2016:3(4):ofw186

A quasi-experimental study conducted by the Antimicrobial Stewardship Program (ASP) at the University of Colorado. The ASP convened a multidisciplinary workgroup to develop a pneumonia guideline and CPOE admission order set for non-ICU CAP. The implementation strategy included electronic dissemination of guidelines to clinicians and multiple educational sessions performed by hospitalists who were part of the workgroup. The guideline recommended a 5-day course of a fluoroquinolone-sparing regimen for uncomplicated pneumonia.

Median duration of therapy decreased from 10 to 7 days (P<0.0001).Levofloxacin prescriptions at discharge decreased from 60% to 27% (P<0.001).

Frequency of clinical failure (a composite outcome of re-admission due to pulmonary infection (1% vs 6%), in-hospital mortality (1% vs 0%), treatment failure (5% vs 4%), recurrence (2% vs 4%), 30-day mortality (0% vs 0%)) was the same pre and post intervention (7% vs 10%; p=.53).

2. Unranga A, Espana P, Bilbao et al. Duration of Antibiotic Treatment in Community-Acquired Pneumonia: A Multicenter Randomized Clinical Trial. JAMA Intern Med. 2016;176(9):1257–65

Randomized Clinical Trial (RCT)–The intervention arm was treated until afebrile for 48 hours and no more than one pneumonia associated instability (per IDSA guidelines), but with a 5-day minimum. The control arm's treatment duration was determined by physicians. Outcomes were clinical success rates (resolution or improvement of signs and symptoms related to pneumonia without further antibiotic therapy) and CAP symptom questionnaire scores. They had planned to look at clinical cure, all-cause mortality, and major complications as the primary outcome but there were too few events. There were no differences in clinical success rates or CAP questionnaire score between intervention and control group. Median treatment duration was 5 days in the intervention group and 10 days in the control group.

There were no significant differences for time until clinical improvement, days to return to normal activity, radiographic resolution (Day 30), adverse effects (Day 30), in-hospital mortality, 30-day mortality, in-hospital complications, recurrence by day 30, and length of hospital stay. Readmission by day 30 was more common in control group (6.6% vs 1.4%, P=0.02).

In the intervention group, 70.1% qualified for and received 5 days of therapy. There were 13/162 protocol violations that were not included in the per protocol analysis. Of the cohort (intervention and control group), 80% were treated with a quinolone, 11% with beta-lactam alone, and 9% with a beta-lactam and macrolide.

3. Avdic E, Cuschinotto LA, Hughes AH, et al. Impact of an antimicrobial stewardship intervention on shortening the duration of therapy for community-acquired pneumonia. Clin Infect Dis 2012;54 (11):1581–7.

Quasi-experimental study performed at Johns Hopkins with education and postprescription review and feedback of treatment provided to patients with CAP.

Treatment duration was 5 days for pneumonia patients without immunocompromising conditions or structural lung disease, 7days for moderately immunocompromised and/or structural lung disease, and 10-14 day for patients with poor clinical response or significantly immunocompromised.

Median duration of therapy went from 10 to 7 days. The Pre-intervention period was in 2008 and at that time 58% of patients received moxifloxacin. The intervention period was in 2010 and 58% received ceftriaxone + azithromycin.

There was no difference in LOS and 30-day re-admission rates were higher in the pre-intervention group (though not statistically significant).

4. Li DX et al. Sustained Impact of an Antimicrobial Intervention for Community-Acquired Pneumonia. Infect Control Hosp Epidemiol 2016; 37:1243-1246.

A follow-up study 3 years after the intervention was performed in Reference 3. There was no difference in length of stay or hospital re-admission compared to the original study period 3 years prior. Median duration of antibiotics for CAP remained at 7 days.

5. Li JZ, Winston LG, Moore DH, Bent S. Efficacy of short-course antibiotic regimens for community-acquired pneumonia: a meta-analysis. Am J Med. 2007;120 (9):783-90.

Meta-analysis: Included 15 RCT and 10/15 used azithromycin, 2/15 beta-lactam, and 2/15 with fluoroquinolones. Only two were specifically about hospitalized patients. There was no difference in clinical failure between shortcourse and extended course regimens. No difference in risk of mortality or bacterial eradication. Subgroup analysis, there was trend toward favorable clinical efficacy for the short course regimens in all antibiotic classes.

Conclusion was that mild-moderate CAP can be safely and effectively treated with an antibiotic regimen of 7 days or less.

6. Leophante P, Choutet P, Gaillat J, et al. Efficacy of a ten-day course of ceftriaxone compared to a shortened five-day course in the treatment of community-acquired pneumonia in hospitalized adults with risk factors. Med Mal Infect 2002; 32:369-81.

French RCT study: Patients were randomized to 5-day IV ceftriaxone followed by 5 day placebo IM versus 5 days IV ceftriaxone followed by 5 days ceftriaxone IM.

The primary criterion for success was being afebrile on day 10. There was no difference between the groups. Secondary criteria was clinical normalization at day 10, cure (clinical/radiological at day 30/45), and absence of new antibiotic starts before day 30/45. Fewer patients had clinical and radiographic normalization in the 10-day treatment group, but other secondary endpoints were not different between treatment arms.

Patients had to also have a risk factor for inclusion—age ≥ 65, tobacco ≥ 10ppd, chronic alcoholism, non-decompensated underlying disease, and malnutrition or obesity. No patients with malignancies or immunosuppression were included.

7. Dimopoulos G, Mathaiou DK, et al. Short versus long-course antibacterial therapy for community-acquired pneumonia: a meta-analysis. Drugs. 2008;68(13):1841–54.

Systematic review which included 5 RCTs for adults. The main outcome for clinical success was defined as complete resolution or improvement of symptoms and signs of CAP which was assessed at the end of therapy evaluation visit.

There was no difference in effectiveness and safety of short versus long course antimicrobial therapy. A subgroup analysis also found no difference for patients treated with no more than 5-day short course vs 7-day long course regimen—but 5 vs 7 included gemifloxacin trial, telithromycin trial, and ceftriaxone trial (see above ref 6).

8. File TM Jr. Mandell LA, et al. Gemifloxacin once daily for 5 days versus 7 days for the treatment of community-acquired pneumonia: a randomized, multicenter, double-blind study. J Antimicrob Chemother 2007;60:112–20.

A double blind, multicenter RCT comparing 5 days versus 7 days of gemifloxacin for CAP. The 5-day treatment arm was non-inferior to 7-day treatment arm with respect to clinical, bacteriological, and radiological efficacy.

9. Moussaoui R, et al. Effectiveness of discontinuing antibiotic treatment after three days versus eight days in mild to moderate-severe community-acquired pneumonia: randomized, double blind study. BMJ 2006;332:1335.

A RCT performed in the Netherlands. The intervention was IV amoxicillin X 3 days followed by no further antibiotics or oral amoxicillin for 5 days. At day 3 of therapy they rated four respiratory symptoms. Patients who had improved by ≥ 2 points on this scale, afebrile, and able to take oral medications were then randomized.

20.4% did not improve enough to be randomized. There was no significant difference in length of stay, clinical cure, bacteriological success, and radiological success at day 10 and day 28.

The study excluded patients with a PSI > 110, severe CAP and immunosuppressed patients (neutropenia, HIV infection with AIDS, ICU, *S.aureus* pneumonia, empyema, primary immunodeficiency, and asplenia).

10. Dunbar LM, Wunderink RG et al. High-dose, short-course levofloxacin for community-acquired pneumonia: a new treatment paradigm. Clin Infect Dis 2003;37:752-60.

A RCT comparing 5 days of levofloxacin 750 mg daily vs 10 days of levofloxacin 500 mg daily. Fevers resolved more frequently at Day 3 in the short course arm. There was no difference in clinical success rates or microbiologic eradication rates.

11. Foolad F, Huang A et al. Impact of a Multi-faceted Stewardship Intervention on Duration of Antibiotic Therapy for the Treatment of Community-Acquired Pneumonia. ID Week; 2016 Oct 26-30; New Orleans, LA. Abstract 1029.

A quasi-experimental study performed at University of Michigan and Medical College of Wisconsin with interim analysis. A stewardship intervention including CAP guideline update, pharmacist education, prescriber education, and prospective audit and feedback was implemented. The recommended duration of therapy was based on IDSA guidelines (applying clinical stability criteria).

There was a significant decrease in the median duration of therapy 7 vs 8 days ($P<0.001$). There was also a decrease use in high risk CDI antibiotics—ceftriaxone, cefpodoxime, and levofloxacin ($P<0.05$).

There was no difference in mortality, length of stay, re-admission for pneumonia, or incidence of CDI. In the abstract 44.4% of patients in the intervention group met criteria for 5 days and 37% received 5 days and 47.3% in the pre-intervention group met criteria for 5 days and 10% received 5 days.

12. Shorr, AF et al. A Mulitcenter, Randomized, Double- Blind, Retrospective Comparison of 5- and 10 day Regimens of Levofloxacin in a Subgroup of Patients Aged > 65 years with Community-Acquired Pneumonia. Clinical Therapeutics 2005. 27;1251-1259.

This study was a subgroup analysis of reference 10 that only included analysis of elderly patients > 65 years (41.3% in the 5 day group had COPD). Clinical success was similar between 5 and 10-day regimens.

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Treatment of Community-Acquired Pneumonia

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Overview

This document details the Hospital Medicine Safety (HMS) consortium recommendations for empiric therapy and duration of treatment for HMS eligible (hospitalized, non-intensive care unit) patients with community acquired pneumonia (CAP).

The treatment recommendations highlighted in this document are not meant to be a comprehensive guideline. Many aspects of the management of CAP are not covered in this document, including items such as appropriate diagnostic testing, criteria for the timing of IV to oral step down, discharge criteria, etc. HMS recommendations regarding these aspects of pneumonia care may subsequently be developed based on findings from ongoing data collection at HMS hospitals, but for now, please refer to national or locally developed CAP guidelines.

Intended Use

- These recommendations are intended for **non-ICU patients** with CAP who are not severely immunosuppressed and do not have risk factors for multidrug-resistant (MDR) organisms (see appendix for select risk factors).
- Hospitals should choose their preferred regimen among the options provided based on antimicrobial stewardship/infectious diseases recommendations, hospital formulary restrictions, and hospital antibiograms.

Empiric Treatment for Community-Acquired Pneumonia

HMS Preferred

- Ampicillin-Sulbactam **PLUS** Azithromycin, Clarithromycin, or Doxycycline
- Ceftriaxone or Cefotaxime **PLUS** Azithromycin, Clarithromycin, or Doxycycline

Alternative but HMS Non-Preferred

- Levofloxacin[1]
- Moxifloxacin[1]

Aspiration Pneumonia

- Anaerobic coverage is not routinely warranted in non-critically ill patients with aspiration pneumonia.
- Anaerobic coverage may be appropriate in patients with cavitary or necrotizing pneumonia, empyema, complicated parapneumonic effusion, lung abscess, or post-obstructive pneumonia. The regimens for appropriate anaerobic coverage are not included in this guideline.

Empiric Oral Step-Down Therapy: When no etiologic pathogen identified for Community-Acquired Pneumonia[2]

Amoxicillin
Amoxicillin/clavulanate
Cefpodoxime
Cefdinir
Cefditoren
Cefuroxime

} +/- Azithromycin, Doxycycline, or Clarithromycin[3]

Alternatives: Levofloxacin, Moxifloxacin in setting of severe PCN allergy

Duration of Therapy[4]

Uncomplicated CAP

- 5 days[5]
- Therapy can be continued for patients who are febrile or clinically unstable[6] on day 5 of treatment

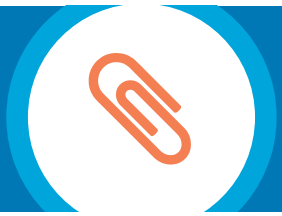
Complicated CAP[7]

- 7 days[8,9]
- Therapy can be continued for patients who are febrile or clinically unstable[6] on day 7 of treatment

Footnotes

1. *Preferred for patients with cephalosporin allergy, allergy to both macrolides and doxycycline/tetracycline, or severe penicillin allergy [hives, angioedema, anaphylaxis, drug reaction with eosinophilia and systemic symptoms (DRESS), stevens-johnson syndrome (SJS), toxic epidermal necrolysis (TENS)]*
2. *If an etiologic organism is identified based on diagnostic testing, we recommend targeted, narrow spectrum treatment using local susceptibility data.*
3. *There is debate regarding the continuation of atypical coverage for clinically improving patients with CAP when legionella, mycoplasma, and chlamydia spp. have not been identified as an etiology. The IDSA/ATS CAP guideline supports the addition of a macrolide or doxycycline to a beta-lactam for initial empiric CAP treatment. However, many studies supporting the addition of atypical coverage focused on therapy administered during the first 24 hours of hospitalization. A large clinical trial has not been performed addressing continuation of atypical coverage beyond 24-72 hrs when an etiology has not been identified. Therefore, clinicians can individualize treatment after clinical improvement taking into account pneumonia severity, patient specific factors, and institution specific preferences.*
4. *Patients with legionella pneumonia, empyema, parapneumonic effusion, cavitary pneumonia, lung abscess, necrotizing pneumonia, thoracic surgery during hospitalization, pleural drainage catheters, bacteremia, or opportunistic infections (e.g. PCP pneumonia) are not addressed in the following recommendations.*
5. *If patient is afebrile for 48 hrs and has no more than 1 sign of clinical instability by day 5 of treatment.*

6. *Signs of clinical instability: oxygen saturation < 90% or new oxygen requirement, heart rate > 100 beats/minute, respiratory rate > 24 breaths/minute, systolic blood pressure < 90 mmHg, altered mental status (different than baseline).*
7. *Patients with structural lung disease (e.g. bronchiectasis, pulmonary fibrosis, interstitial lung disease), moderate/severe COPD (excluding COPD exacerbation without pneumonia), documented pneumonia with MRSA, MSSA, or pseudomonas (or other non-fermenting gram-negative pneumonia), or immunosuppressed.*
8. *If patient is afebrile for 48 hrs and has no more than 1 sign of clinical instability by day 7 of treatment. Note: azithromycin duration should be no more than 5 days.*
9. *Some experts recommend 7 days of therapy for immunosuppressed patients and patients with structural lung disease or moderate/severe COPD. However, data supporting 5 days versus 7 days of therapy for such patients is lacking and either duration would be considered appropriate assuming criteria for clinical stability is met.*



Appendix

Suggested Antibiotic Dosing[1]:

Drug Name	Dose	Route	Frequency
Amoxicillin	1 g	PO	3 x daily
Amoxicillin/clavulanate XR	875 mg - 2 g	PO	2 x daily
Ampicillin Sulbactam	3 g	IV q	6 hours
Azithromycin	500 mg 250 mg	PO/IV q 24	on day 1 once daily x 4 days
Cefdinir	300 mg	PO	2 x daily
Cefditoren	400 mg	PO	2 x daily
Cefotaxime	1 g	IV q	8 hours
Cefpodoxime	200 mg	PO	2 x daily
Ceftriaxone	1 g	IV q	24 hours
Cefuroxime	500 mg	PO	2 x daily
Clarithromycin	500 mg	PO	2 x daily
Doxycycline	100 mg	PO	2 x daily
Levofloxacin	750 mg	PO/IV	1 x daily
Moxifloxacin	400 mg	PO/IV	1 x daily

1. *Suggested dosing only. Please individualize based on renal function or other pertinent clinical factors.*

Select Risk Factors for MDR Organisms

- Coming from a nursing home or long term care facility
- Hospitalized ≥ 2 days in the last 90 days
- IV chemotherapy, IV antibiotics, home wound care, or hemodialysis in the 30 days prior to admission

Severely Immunosuppressed

- AIDS (CD4 count < 200 cells/microL)
- Neutropenia (ANC ≤ 0.5 K/uL)
- Cystic fibrosis
- Solid organ and bone marrow transplant recipients
- Receiving 2 or more immunosuppressive agents
- Congenital or acquired immunodeficiency, except HIV positive with CD4 > 200

HMS GUIDELINES HAVE SINCE BEEN UPDATED TO REFLECT UPDATED 2019 CAP Guideline

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Each year HMS reviews the current collaborative performance to determine thresholds for the following years performance measures. A strict process is followed to ensure a standardized regimen for setting performance thresholds. Using the most recent completed quarter of collaborative data, each measure is assessed identifying the threshold that corresponds to the top 25%, 33% and 50% of hospitals for both the full point, partial points and no points threshold. Please see the example below:

Measure: Increase Use of 5 Days of Antibiotic Treatment in Uncomplicated CAP (Community Acquired Pneumonia) Cases (i.e. reduce excess durations)			
	Top 25% of Hospitals	Top 33% of Hospitals	Top 50% of Hospitals
Full Point Threshold	>50%	>44%	>39%
Partial Points Threshold	35-48%	35-43%	30-38%
No Points Threshold	<35%	<35%	<30%

For each point threshold, the threshold that corresponds to the top 25% of hospitals is assessed first as our goal is to continue to improve performance year over year. Subsequently, the threshold is assessed to ensure that it is representative of at least 10% of the patients in the cohort for methodologic rigor[1]. Lastly, taking into account feedback from collaborative members and clinical leadership, each threshold is assessed to determine if there are unintended consequences, limitations in data collection, or gaps in performance due to clinical judgement, which would impact the threshold determination. During the course of the year, collaborative members review their cases which provides an understanding of the improvement opportunity. If the threshold that corresponds to the top 25% of hospitals is not determined to be appropriate based on the process noted above, the same process will be followed for the top 33% and 50% of hospitals.

References

1. Weissman, et al. Achievable benchmarks of care: the ABCs of benchmarking. Journal of Evaluation in Clinical Practice. 1999: 5(3) pp.269-281

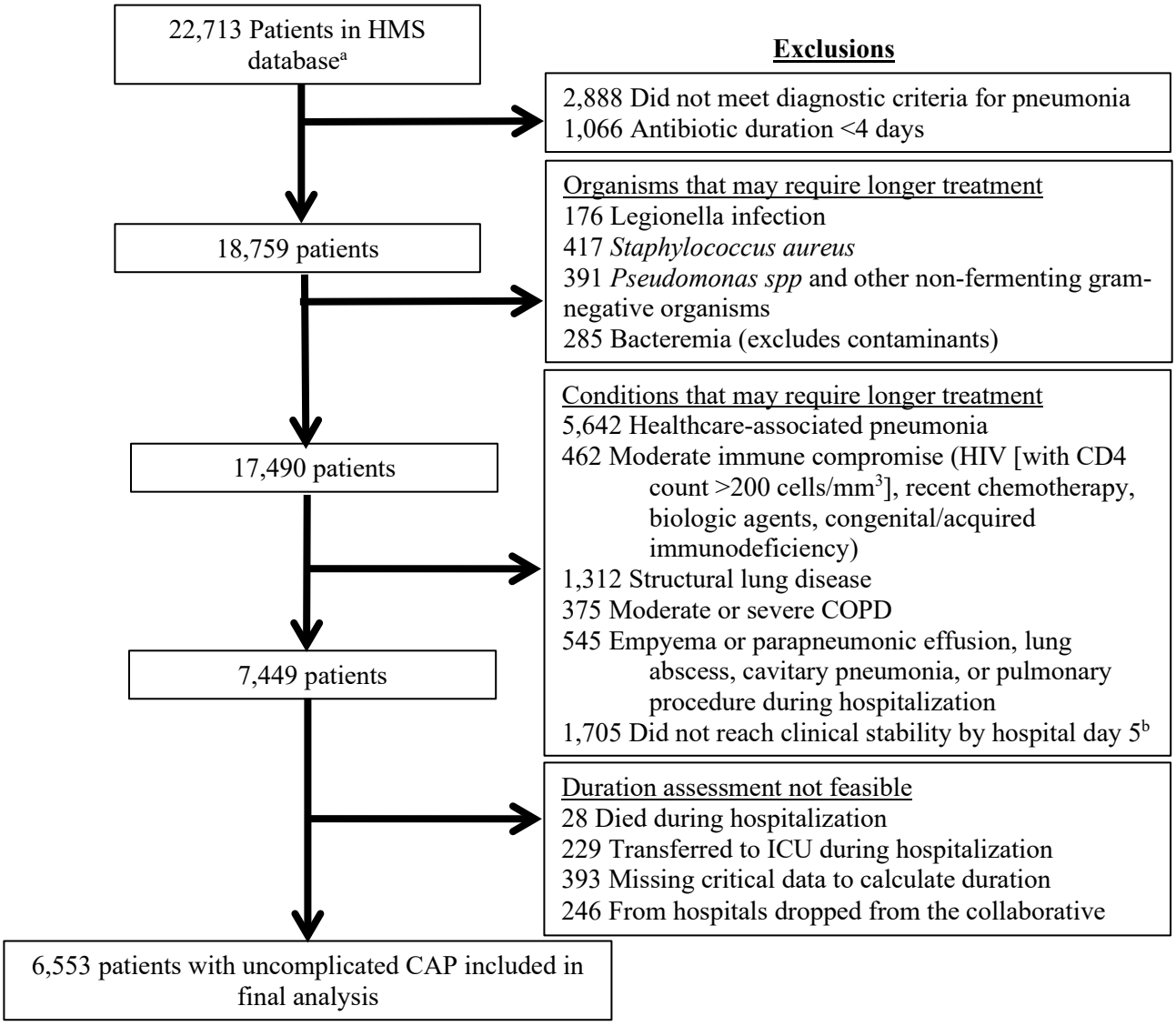
Signs, Symptoms, and Chest Imaging Findings Consistent with Pneumonia

Michigan Hospital Medicine Safety Consortium Pneumonia Definition	
Patient had to meet radiographic component and have 2 or more clinical findings	
Radiographic Component[1]	**Clinical Findings**
Air space density/opacity/disease	New or increasing cough
Bronchopneumonia	Sputum production or change in character of sputum
Cannot rule out pneumonia	New or increased dyspnea OR tachypnea (respiratory rate >20 or physician documentation)
Cavitation	Hypoxemia (Oxygen saturation <90% OR partial pressure of arterial oxygen <60 mmHg
Consolidation	Fever (≥38)C or hypothermia (<36.1C)
Ground glass[2]	Exam consistent with pneumonia (rales, crackles dullness on percussion, bronchial breath sounds, or egophony)
Infection (cannot rule out infection, likely infection)	
Infiltrate (single lobe, multiple, not specified, new or worsening)	White blood cell count <4,000 K/uL OR >10,000 K/uL OR >15% bands (immature neutrophils)
Loculations	
Mass[3]	
Nodular airspace disease[4]	
Pleural efusion[5]	
Pneumonia, aspiration pneumonia[6], necrotizing pneumonia & post-obstructive pneumonia	
Tree in bud[7]	

1. If interval improvement/resolution, no change from previous/no interval change, normal/no abnormalities or no evidence of pneumonia is documented the patient is considered not to have pneumonia and is excluded.
2. If interstitial lung disease, pulmonary edema or pulmonary vascular congestion is documented the patient is considered not to have pneumonia and is excluded.
3. If neoplasm/metastatic disease/malignancy is documented the patient is considered not to have pneumonia and is excluded.
4. If neoplasm/metastatic disease/malignancy or interstitial lung disease is documented the patient is considered not to have pneumonia and is excluded.
5. If pulmonary edema, pulmonary vascular congestion, or ground glass is documented the patient is considered not to have pneumonia and is excluded.
6. If pneumonitis is documented the patient is considered not to have pneumonia and is excluded.
7. If neoplasm/metastatic disease/malignancy or interstitial lung disease is documented the patient is considered not to have pneumonia and is excluded.

The diagnosis of pneumonia is assessed using a combination of chest CT, chest X-Ray and abdominal CTs. All images from -1 to +3 days from admission are included and any positive image (based on algorithm above) in this timeframe is considered pneumonia. Patients not meeting criteria for pneumonia are excluded from this study.

eFigure 2. Flow Diagram for Patient Inclusion



[a]Patients potentially eligible for inclusion in the HMS database were identified based on presence of a discharge diagnostic code of pneumonia and receipt of antibiotics on day 1 or 2 of hospitalization. Patients not eligible for inclusion were those with any of the following: concomitant infection, initial admission to the ICU, pregnancy, severe immune compromise (e.g., AIDS), mycobacterial or fungal infection (i.e., documented fungal pneumonia, mycobacterium/mycobacterial infection, tuberculosis and/or aspergillus/Aspergillosis during the hospital encounter).

[b]For this analysis, patients in the HMS database were excluded if they did not have uncomplicated CAP with an expected antibiotic duration of 5 days. Thus, patients with organisms or conditions that may require longer duration were excluded as well as patients where duration assessment was not feasible. This includes patients who did not reach clinical stability by day 5. Clinical stability was defined as being afebrile (temperature <37.9 °C) for ≥48 h and having ≤1 sign of clinical instability (heart rate >100 beats/min, respiratory rate >24 breaths/min, systolic blood pressure <90 mm Hg, arterial saturation <90% on room air or oxygen requirement higher than at baseline, or mental status altered from baseline). Patients were also considered clinically unstable if oxygen requirement on day 5 (or discharge) was higher than baseline or ≥ 3 L.

Abbreviations: HMS, Michigan Hospital Medicine Safety Consortium; CAP, community-acquired pneumonia, HIV, human immunodeficiency virus, COPD, chronic obstructive pulmonary disease, ICU, intensive care unit, AIDS, acquired immunodeficiency syndrome

Michigan Hospital Medicine Safety (HMS) Collaborative
Data Curation Methods – General

Details on the HMS Databases

Relevant to this manuscript, HMS has a database related antimicrobial use (ABX). The database is used as the primary hub of case abstraction, data reporting, case volume analysis, resource gathering and abstraction queries. All of the HMS databases use both Drupal and LimeSurvey software for data collection/abstraction, which are maintained by the HMS Coordinating Center and our database administrative team. For data reporting, HMS uses Business Objects software to allow hospitals participating in HMS to access their updated data on a daily basis.

For resource gathering and abstraction queries, HMS utilizes a link to a Zendesk guide, which allows abstractors to submit questions regarding data abstraction/reporting, obtain updated data definitions and access resources and quality improvement tools.

Upgrades

Upgrades to the HMS databases occur at least once per year. Upgrades may occur more frequently, depending on updates made to the project throughout the year and changing data needs for quality improvement projects. During an upgrade, the HMS database undergoing updates is taken offline and is unavailable for data abstraction. Upgrades may occur if we have spelling or grammatical errors to fix, selections to add or remove, questions to add or remove, branching questions to add or remove, and/or functionalities to improve or update. After completion of an upgrade, data entered prior to the upgrade is archived and restored in the database. If new questions are added, the abstractors are not expected to return to previously entered cases to enter new data fields as case entry can span several years. The HMS Coordinating Center tracks all updates using a ticketing system and the data analytics and statistician team are made aware of all updates.

Data Validation: Audits

Audits are conducted to ensure that the data is being collected consistently across all participating hospitals. The goal is to identify issues with the abstraction process so that they can be appropriately addressed via education and/or changes to the data entry system. Each HMS-participating hospital is audited by a trained member of the Coordinating Center at least once per year. On average ~50 audits have been conducted per year since the launch of HMS in 2011. This number increases each year as new hospitals join the collaborative. It is the expectation that each audited site will attain a 95% or greater rate of accuracy to receive full points on the HMS Performance Index. To determine the audit score, the auditor calculates a score for each individual case based on the average number of audit fields as noted below (see Medical Record Review). Then using the individual scores for each case, an overall audit score is calculated by averaging all of the audit cases combined. If a site receives a score of less than 95% on an audit, every attempt will be made to re-audit that site in the same year.

The audit consists of four parts: medical record review, review of eligibility lists, review of inclusion/exclusion criteria and practices, and post-audit follow up.

Medical Record Review:

The primary focus of the audit is a medical record review of pre-selected cases by one to three HMS auditors. For each initiative, key complication cases are required to be audited to ensure accurate outcome measures for reporting purposes. For pneumonia, a review of Clostridioides difficile complications is required. Prior to the audit, the primary auditor queries the data analytics team to obtain the list of required complication cases that are due for audit and a random sample of additional non-complication cases. On average 7 to 10 cases are audited if one auditor is present. If a site has a large number of unaudited complication cases, a second or third auditor will join to complete additional cases. The list of cases is distributed to the abstractor 1 to 2 weeks in advance of the audit. Prior to sending the list of audited cases, the abstractor is locked from making updates to previously completed cases. Upon the on-site audit, the auditor(s) independently reviews the medical documentation for each case from the hospital's Electronic Medical Record (EMR) and compares it to what was entered into the HMS database. At the end of the audit day, the auditor's case findings and discrepancies between the EMR and the information entered into the HMS databases (if applicable) will be reviewed in detail with the abstractor. At the resolution of the audit, these discrepancies (if validated as incorrect by both the abstractor and auditor), are corrected in the database by the abstractor to ensure case accuracy. The auditor will also provide additional education, as needed, as issues are identified. If during the medical record review a completed eligible case is determined by the auditor to be ineligible, a score of 90% is assigned to the case and added to the overall average score. The average number of fields that are audited per case per case for pneumonia is 2,072.

Eligibility List Review:

The second item reviewed during an audit is the eligibility/discharge lists and coding at the site being audited. Prior to the audit, the abstractor connects with their hospital's information technology (IT) group for the coding used to generate their eligibility/discharge lists for Pneumonia. This coding is reviewed by the auditor and feedback is provided regarding updates that need to be made to the coding, if applicable.

Inclusion/Exclusion Criteria Review:

The final item reviewed during an audit is inclusion/exclusion criteria. The purpose of this review is to ensure that the abstractor understands the inclusion/exclusion criteria for each project and is applying those criteria appropriately when reviewing cases. At least one case for each project deemed ineligible by the abstractor is randomly selected and reviewed with the auditor(s). Once a case is identified, the abstractor shows the auditor(s), in the medical record, the reason the case was excluded from abstraction. If a case was deemed ineligible by the abstractor, but was determined through this review that it was actually eligible for abstraction, another case from the same project will be reviewed until a legitimate ineligible case is found. If the abstractor has incorrectly identified a case as ineligible, the auditor(s) will provide additional on-site education about eligibility criteria. If more than 2 randomly-selected cases were deemed ineligible by the abstractor, but are determined to be eligible for abstraction after review, a score of 90% will be added to the final audit summary for each additional case that is found to be eligible.

Post-Audit Follow Up:

After the audit has concluded, the primary auditor composes a summary of the findings, including specific areas to update in the HMS databases, education provided to the site during the audit, and a summary of any findings from the eligibility/discharge list review. The final audit summary is provided to the site within two to three weeks of completion of the audit. This summary will be sent to the site's abstractor(s), quality administrator, and physician champion. The summary will include a percentage score for the audit, which is calculated based on the average of the scores for all cases reviewed. Upon receiving the final audit summary, the abstractor(s) has three months from the date of receipt to make all updates in the HMS database noted in the final report. The final audit score is then factored into the site's performance index scorecard for the given year. During a typical year, 5% of the performance index is associated with the audit score(s) completed during the performance year.

Data Validation: Data Checker

Each HMS database has a robust data checker that can identify in real time errors in abstraction that have occurred on a case-by-case basis. Abstractors are trained to run a data checker on each case before submitting it to the database so that any data errors are identified at the time of the initial abstraction and can be corrected prior to submission. Additionally, a live daily report is available, which provides a culmination of all data errors on all cases entered into the database that an abstractor is able to see in order to correct potential discrepancies in data abstraction.

The ABX database has a total of 226 individual checks. These data checks range from potential length of stay issues (i.e., a case where the length of stay = 1) to verification that cultures are appropriately entered (i.e., it was noted in a form that a respiratory culture was collected, but no respiratory culture form was completed for that case). The data checker is also utilized to highlight which days in our Daily Entry tab need to be completed for that case. As a note, the "Daily Entry tab" is the section of forms that are utilized to enter daily antibiotic and vital sign information for ABX cases. After the entry of all data forms, the abstractor runs the data checker for that case and upon completion of the data checker validation, the Daily Entry tab days that need to be completed are highlighted in red and all days that do not need to be completed remain gray. This allows the abstractors to know exactly which days need to be entered and verify that they have fully completed data abstraction for that case.

Data Validation: Global Data Checks

The HMS Coordinating Center conducts global data checks on an ad hoc basis during the data analysis process to identify any issues that might occur across the entire database that may not be included in the data checker. These global data checks are typically run when we identify an error as part of another process, such as coding a report and realizing something does not pull into the report as expected. The HMS Coordinating Center will do data queries to sites throughout the year with prompts to analyze their data in accordance with the medical record if we notice discrepancies outside of the data checker elements.

Data Validation: Site Specific

Each hospital receives site specific data reports via a printed version quarterly and daily within the database/registry. Included in these reports are the sites overall score for each measure by quarter and a detailed list of cases that have been identified as opportunities for improvement (i.e., also titled fall-

outs). Each hospital is encouraged to review these fall-outs with their local team to perform audit and feedback, identify trends, and assist with overall quality improvement. Occasionally, during this review the local team will identify a potential issue with how the fall-out was determined based on the clinical scenario. In some instances, the case is reviewed and justification for the coding/calculation is reinforced to the local site. In other instances, modifications to the code and/or additional modifications to the data registry questions are required. Typically, the latter is more common at the initial launch of a new measure. For more longstanding measures, modifications are rare.

Michigan Hospital Medicine Safety Consortium Data Sources for Hospital Characteristics

Academic Hospital Status: Data obtained from the American Hospital Association's (AHA) Data Hub. Hospitals were classified as academic if any of the following were reported: medical school affiliation reported to the American Medical Association, residency training approved by the Accreditation Council for Graduate Medical Education, or Member of Council of Teaching Hospitals of the Association of American Medical Colleges. Retrieved 04/28/2021 from https://guide.prod.iam.aha.org/guide/searchResults

Ownership Status: Data obtained from AMA's Data Hub. Retrieved 04/28/2021 from https://guide.prod.iam.aha.org/guide/searchResults

Bed Size: Data obtained from 2019 Michigan Certificate of Need Annual Survey, Basic Total Licensed Beds Utilization Statistics. Retrieved 4/21/2021 from https://www.michigan.gov/documents/mdhhs/Report_010_Hospital_Beds_by_HSA_703357_7.pdf

Number of Hospitalists: For hospitals still participating in the Michigan Hospital Medicine Safety Consortium, data are self-reported from the November 2019 hospital survey. For non-participants, data were collected from hospital websites.

System Status: data obtained from Michigan Health and Hospital Association; Michigan Hospitals by Health System. Retrieved 04/19/2021 from https://www.mha.org/About/Our-Hospitals/Michigan-Hospitals-By-Health-System

Michigan Hospital Medicine Safety (HMS) Collaborative
Definition of sex, race, ethnicity

Gender

Instructions: Review the medical record to determine the gender of the patient.
This is a required field and the form cannot be submitted without an entry in this field.
Select one of the following:

- *"Male"* if the patient is categorized as a man in the medical record.
- *"Female"* if the patient is categorized as a woman in the medical record.
- *"Unknown"* if the patient's gender is unknown.

Ethnicity

Instructions: Review the medical record to determine the patient's ethnicity.
Select one of the following:

- *"Hispanic or Latino"* if patient demographic information indicates patient is of Hispanic descent. The US Census Bureau states that "People who identify their origin as Spanish, Hispanic, or Latino may be of any race."
- *"Non-Hispanic or Latino"* if patient demographic information indicates patient is not of Hispanic descent.
- "*Unknown*" if ethnicity is not reported in the medical record.

Race

Instructions: Review the medical record to determine the patient's race.
Select one of the following:

- *"American Indian or Alaskan Native"* if patient demographic information indicates patient is Native American, American Indian, or Alaska Native.
- *"Arab and Chaldean Ancestries"* if the patient demographic information indicate patient is of Arab or Chaldean Ancestries.
- *"Asian"* if patient demographic information indicates Asian.
- *"Black or African American"* if patient demographic information indicates patient is black or African American.
- *"Native Hawaiian or Pacific Islander"* if patient demographic information indicates patient is Native Hawaiian or Pacific Islander.
- *"White or Caucasian"* if patient demographic information indicates patient is white or Caucasian.
- *"Other"* if patient demographic information indicates the patient is a race other than what is listed above.
- *"Unknown"* if patient's race is not indicated in the medical record.

Patient Characteristics Used for Adjustment in Clinical Outcome Analyses

Composite outcome, mortality, readmission, and urgent visit* were adjusted for age, Charlson comorbidity index, sex, Pneumonia severity index, length of stay, Medicaid insurance, and concurrent disease exacerbations (chronic obstructive pulmonary disease, heart failure).

Clostridioides difficile infection was adjusted for age, Charlson comorbidity index, inflammatory bowel disease, immunosuppression medications, tube feeds, proton pump inhibitor, length of stay, antibiotic use in the prior 90 days, and number of antibiotics in prior 90 days.

Physician-reported adverse events were adjusted for age, Charlson comorbidity index, and sex.

Patient reported adverse events were adjusted for age, Charlson and sex. Patient-reported adverse drug events were obtained via 30-day follow-up phone call. Of the 6669 patients contacted to ascertain patient-reported adverse events, 3888 (58.3%) responded.

*Urgent visit includes any urgent visit not resulting in hospitalization including emergency department visit, urgent care visit, or observation stay.

Revised Standards for Quality Improvement Reporting Excellence (SQUIRE 2.0)
September 15, 2015

Text Section and Item Name	Section or Item Description	
Notes to authors	• The SQUIRE guidelines provide a framework for reporting new knowledge about how to improve healthcare • The SQUIRE guidelines are intended for reports that describe system level work to improve the quality, safety, and value of healthcare, and used methods to establish that observed outcomes were due to the intervention(s). • A range of approaches exists for improving healthcare. SQUIRE may be adapted for reporting any of these. • Authors should consider every SQUIRE item, but it may be inappropriate or unnecessary to include every SQUIRE element in a particular manuscript. • The SQUIRE Glossary contains definitions of many of the key words in SQUIRE. • The Explanation and Elaboration document provides specific examples of well-written SQUIRE items, and an in-depth explanation of each item. • Please cite SQUIRE when it is used to write a manuscript.	**As you review the manuscript, place a checkmark in this column for each SQUIRE item that is appropriately addressed in the manuscript. Remember that not every item is necessary in every manuscript.**
Title and Abstract		
1. Title	Indicate that the manuscript concerns an initiative to improve healthcare (broadly defined to include the quality, safety, effectiveness, patient-centeredness, timeliness, cost, efficiency, and equity of healthcare)	Page 1
2. Abstract	a. Provide adequate information to aid in searching and indexing b. Summarize all key information from various sections of the text using the abstract format of the intended publication or a structured summary such as: background, local problem, methods, interventions, results, conclusions	Pages 3 & 4

Introduction	*Why did you start?*	
3. Problem Description	Nature and significance of the local problem	Page 5
4. Available knowledge	Summary of what is currently known about the problem, including relevant previous studies	Page 5
5. Rationale	Informal or formal frameworks, models, concepts, and/or theories used to explain the problem, any reasons or assumptions that were used to develop the intervention(s), and reasons why the intervention(s) was expected to work	Page 5
6. Specific aims	Purpose of the project and of this report	Page 5
Methods	*What did you do?*	
7. Context	Contextual elements considered important at the outset of introducing the intervention(s)	Pages 6 & 7
8. Intervention(s)	a. Description of the intervention(s) in sufficient detail that others could reproduce it b. Specifics of the team involved in the work	Page 5 & 6 and appendix
9. Study of the Intervention(s)	a. Approach chosen for assessing the impact of the intervention(s) b. Approach used to establish whether the observed outcomes were due to the intervention(s)	Pages 7 & 8
10. Measures	a. Measures chosen for studying processes and outcomes of the intervention(s), including rationale for choosing them, their operational definitions, and their validity and reliability b. Description of the approach to the ongoing assessment of contextual elements that contributed to the success, failure, efficiency, and cost c. Methods employed for assessing completeness and accuracy of data	Pages 6-8
11. Analysis	a. Qualitative and quantitative methods used to draw inferences from the data b. Methods for understanding variation within the data, including the effects of time as a variable	Pages 8 & 9
12. Ethical Considerations	Ethical aspects of implementing and studying the intervention(s) and how they were addressed, including, but not limited to, formal ethics review and potential conflict(s) of interest	Page 9

Results	*What did you find?*	
13. Results	a. Initial steps of the intervention(s) and their evolution over time (*e.g.*, time-line diagram, flow chart, or table), including modifications made to the intervention during the project b. Details of the process measures and outcome c. Contextual elements that interacted with the intervention(s) d. Observed associations between outcomes, interventions, and relevant contextual elements e. Unintended consequences such as unexpected benefits, problems, failures, or costs associated with the intervention(s). f. Details about missing data	Pages 6-8 eFigure 1 eTable 3 Page 11
Discussion	*What does it mean?*	
14. Summary	a. Key findings, including relevance to the rationale and specific aims b. Particular strengths of the project	Pages 11 &12
15. Interpretation	a. Nature of the association between the intervention(s) and the outcomes b. Comparison of results with findings from other publications c. Impact of the project on people and systems d. Reasons for any differences between observed and anticipated outcomes, including the influence of context e. Costs and strategic trade-offs, including opportunity costs	Pages 12 &13
16. Limitations	a. Limits to the generalizability of the work b. Factors that might have limited internal validity such as confounding, bias, or imprecision in the design, methods, measurement, or analysis c. Efforts made to minimize and adjust for limitations	Pages 13 & 14
17. Conclusions	a. Usefulness of the work b. Sustainability c. Potential for spread to other contexts d. Implications for practice and for further study in the field e. Suggested next steps	Page 14
Other information		
18. Funding	Sources of funding that supported this work. Role, if any, of the funding organization in the design, implementation, interpretation, and reporting	Pages 4 & 15

eTable 1. Characteristics of Participating Hospitals vs. Hospitals that Dropped Out During the Study Period

Variable	Participants (n=41)	Dropped Out (n=6)	P-value
Academic hospital, N (%)[a]	35 (85.4%)	5 (83.3%)	0.90
Number of hospitalists, median (IQR)[b]	14 (8-22)	17.5 (13-26)	0.56
Profit Type, N(%)[c]			
Non-profit	34 (82.9%)	6 (100%)	0.99
For profit	5 (12.2%)	0 (0%)	
Governmental	2 (4.9%)	0 (0%)	
Bed Size, N(%)[d]			
Median (IQR)	310 (186-443)	220 (118-379)	0.26
51-100 beds, N (%)	5 (12.2%)	1 (16.7%)	0.99
101-200 beds, N (%)	8 (19.5%)	1 (16.7%)	
>200 beds, N (%)	28 (68.3%)	4 (66.7%)	
Percentage of patients with CAP eligible for 5-day duration who received 5 days (First quarter of participation)	19.0% (10.5-34.4)	18.5% (10.0-26.3)	0.43

Hospitals that participated for at least one year in the Michigan Hospital Medicine Safety Consortium and are included in our study are compared to hospitals that dropped out. P-values were calculated from chi-squared tests with $P<0.05$ considered significant. Abbreviations: IQR, inter-quartile range; ASP, antimicrobial stewardship program

[a] Academic hospital status from the American Medical Association's FREIDA Institution Directory

[b] For participating hospitals, data are self-reported from the November 2019 hospital survey. For non-participants, data were collected from hospital websites.

[c] Profit status obtained from data.medicare.gov.

[d] Hospital bed size was obtained from the 2015 Michigan Certificate of Need Annual Survey.

eTable 2. Patient Characteristics

Variable	Entire Cohort (n=6,560)	Appropriate 5 ±1 Day Duration (n=2,230)	Excess (>6 day) Duration (n=4,330)
Demographics			
Sex; N (%)			
Female	3349 (51.1%)	1136 (50.9%)	2213 (51.1%)
Male	3211 (48.9%)	1094 (49.1%)	2117 (48.9%)
Age; Median (IQR)	67.7 (54.9-80.1)	68.3 (55.9-81.1)	67.4 (54.4-79.5)
Race; N (%)			
Black or African American	1347 (20.5%)	482 (21.6%)	865 (20.0%)
White or Caucasian	4924 (75.1%)	1658 (74.3%)	3266 (75.4%)
Asian	41 (0.6%)	13 (0.6%)	28 (0.6%)
Other[a]	132 (2.0%)	44 (2.0%)	88 (2.0%)
Unknown[a]	116 (1.8%)	33 (1.5%)	83 (1.9%)
Ethnicity; N (%)			
Non-Hispanic	5439 (82.9%)	1911 (85.7%)	3528 (81.5%)
Hispanic	120 (1.8%)	46 (2.1%)	74 (1.7%)
Unknown[a]	1001 (15.3%)	273 (12.2%)	728 (16.8%)
Skilled nursing facility prior to hospitalization; N (%)	68 (1.0%)	29 (1.3%)	39 (0.9%)
Charlson Comorbidity Index Score; Median (IQR)	2 (0-4)	2 (1-4)	2 (0-4)
Comorbidities, N (%)			
Congestive heart failure	1257 (19.2%)	485 (21.7%)	772 (17.8%)
Mild chronic obstructive pulmonary disease	2075 (31.6%)	668 (30.0%)	1407 (32.5%)
Cancer	1071 (16.3%)	383 (17.2%)	688 (15.9%)
Diabetes mellitus	1836 (28.0%)	649 (29.1%)	1187 (27.4%)
Cardiovascular disease	2528 (38.5%)	916 (41.1%)	1612 (37.2%)
Moderate or severe chronic kidney disease	1602 (24.4%)	580 (26.0%)	1022 (23.6%)
Moderate or severe liver disease	61 (0.9%)	25 (1.1%)	36 (0.8%)
Smoking history; N (%)			
Never	2411 (36.8%)	795 (35.7%)	1616 (37.3%)
Prior	2233 (34.0%)	794 (35.6%)	1439 (33.2%)
Current/Active	1843 (28.1%)	621 (27.8%)	1222 (28.2%)
Unknown	73 (1.1%)	20 (0.9%)	52 (1.2%)
Disease Severity			
CURB-65 score; Median (IQR)[b]	2 (1-3)	2 (1-3)	2 (1-3)
Pneumonia Severity Index;[c] N (%)			
Class I: <50	826 (12.6%)	253 (11.3%)	573 (13.2%)
Class II: 51-70	1206 (18.4%)	392 (17.6%)	814 (18.8%)
Class III: 71-90	1525 (23.2%)	510 (22.9%)	1015 (23.4%)
Class IV: 91-130	2256 (34.4%)	804 (36.1%)	1452 (33.5%)

Variable	Entire Cohort (n=6,560)	Appropriate 5 ±1 Day Duration (n=2,230)	Excess (>6 day) Duration (n=4,330)
Class V: >130	745 (11.4%)	270 (12.1%)	475 (11.0%)
Received high-risk antibiotic in prior 90 days;[d] N (%)	692 (10.5%)	181 (8.1%)	511 (11.8%)
Time to clinical stability (days); Median (IQR)[e]	3 (3-3)	3 (3-3)	3 (3-3)
Length of stay (days); Median (IQR)	4 (3-5)	4 (3-5)	4 (3-5)
Diagnostic Testing			
Positive respiratory culture in 90 days prior to hospitalization; N (%)	170 (2.6%)	45 (2.0%)	125 (2.9%)
Respiratory culture or non-culture test; N (%)[f]			
Not Performed	2864 (43.7%)	1054 (47.3%)	1810 (41.8%)
Negative	3176 (48.4%)	1030 (46.2%)	21246 (49.6%)
Any Positive	520 (7.9%)	146 (6.5%)	374 (8.6%)
Antibiotic Use			
Total antibiotic duration (days), Median (IQR)	7 (6-9)	5 (5-6)	9 (8-10)
Empiric antibiotic agent (hospital day 1 or 2); N (%)			
Ceftriaxone	5104 (77.8%)	1802 (80.8%)	3303 (76.3%)
Azithromycin	4693 (71.5%)	1740 (78.0%)	2953 (68.2%)
Levofloxacin	1078 (16.4%)	297 (13.3%)	781 (18.0%)
Doxycycline	932 (14.2%)	233 (10.4%)	699 (16.1%)
Vancomycin	680 (12.0%)	176 (7.9%)	504 (11.6%)
Cefepime	416 (6.3%)	107 (4.8%)	309 (7.1%)
Piperacillin-tazobactam	415 (6.3%)	97 (4.4%)	318 (7.3%)
Ampicillin-sulbactam	284 (4.3%)	100 (4.5%)	184 (4.2%)
Metronidazole	148 (2.3%)	50 (2.2%)	98 (2.3%)
Moxifloxacin	91 (1.4%)	26 (1.2%)	65 (1.5%)
Ciprofloxacin	18 (0.3%)	6 (0.3%)	12 (0.3%)
Other	366 (5.6%)	111 (5.0%)	255 (5.9%)
Discharge Antibiotic Use			
Discharged on antibiotics, N (%)	5575 (85.0%)	1464 (65.7%)	4111 (94.9%)
Discharge antibiotic duration (days), Median (IQR)	4 (2-5)	2 (0-3)	5 (4-7)
Oral antibiotic agent prescribed on discharge, N (%)			
Azithromycin	1816 (27.7%)	721 (32.3%)	1095 (25.3%)
Oral cephalosporin	1666 (25.4%)	502 (22.5%)	1164 (26.9%)
Levofloxacin	1501 (22.9%)	278 (12.5%)	1223 (28.2%)
Amoxicillin-clavulanate	816 (12.4%)	183 (8.2%)	633 (14.6%)
Doxycycline	592 (9.0%)	116 (5.2%)	476 (11.0%)
Moxifloxacin	231 (3.5%)	53 (2.4%)	178 (4.1%)

Variable	Entire Cohort (n=6,560)	Appropriate 5 ±1 Day Duration (n=2,230)	Excess (>6 day) Duration (n=4,330)
Penicillin/Amoxicillin	85 (1.3%)	36 (1.6%)	49 (1.1%)
Metronidazole	41 (0.6%)	5 (0.2%)	36 (0.8%)
Ciprofloxacin	26 (0.4%)	5 (0.2%)	21 (0.5%)

[a] Other race includes American Indian or Alaskan Native, Arab and Chaldean Ancestries, Native Hawaiian or Pacific Islander, and any other race not including any of the above. Unknown race/ethnicity indicates that the patient's race/ethnicity was not indicated in the medical record.

[b] Includes confusion, blood urea nitrogen >19 mg/dl (>7 mmol), respiratory rate ≥ 30, systolic blood pressure <90 mmHg or diastolic blood pressure ≤60 mmHg, and age ≥ 65. Higher scores indicate more severe disease.

[c] Includes age, sex, comorbidities, vital sign and laboratory abnormalities, and pleural effusion on imaging. Higher scores indicate more severe disease.

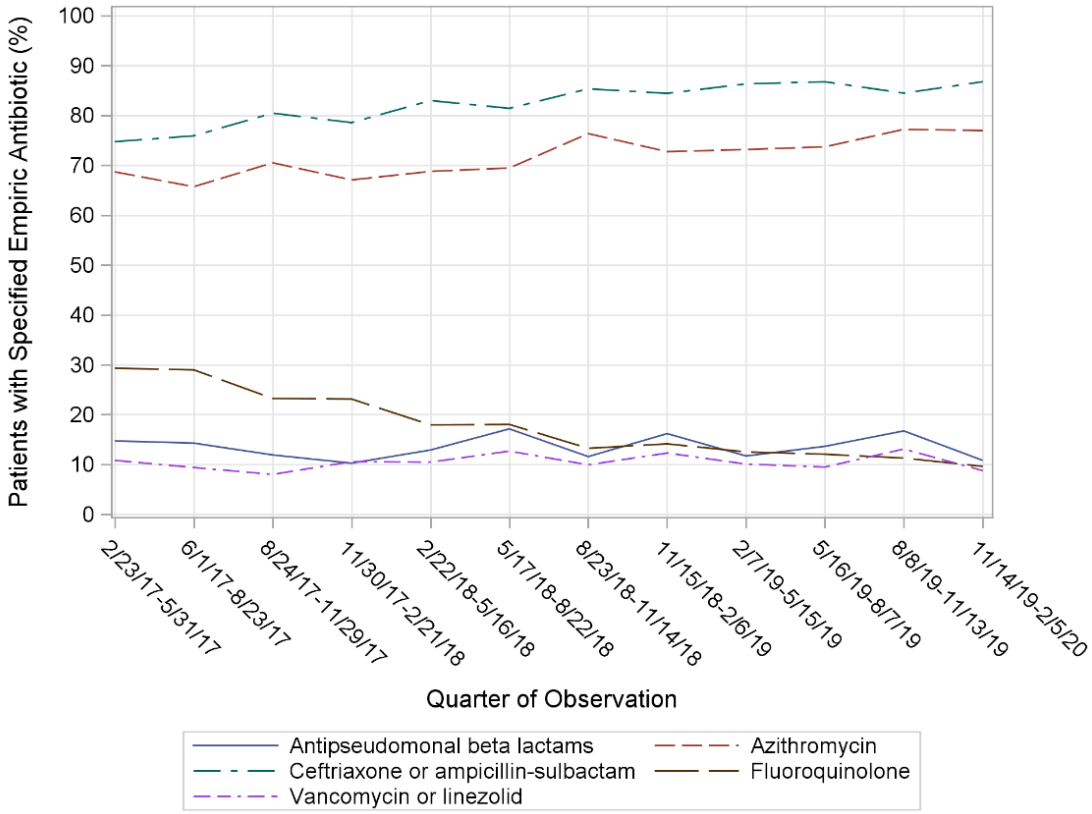
[d] Includes any intravenous antibiotic, any fluoroquinolone, or linezolid, given that these are associated with increased risk for multidrug-resistant organisms or are active against methicillin-resistant *Staphylococcus aureus* or *Pseudomonas* species.

[e] Clinical stability is defined as being afebrile (temperature <37.9 °C) for ≥48 h and having ≤1 sign of clinical instability (heart rate >100 beats/min, respiratory rate >24 breaths/min, systolic blood pressure <90 mm Hg, arterial saturation <90% on room air or oxygen requirement higher than at baseline, or mental status altered from baseline).

[f] Includes respiratory culture or Gram stain, urine *Streptococcus pneumoniae* or *Legionella pneumophila* antigen test, bacterial pathogen identified via polymerase chain reaction, or *Mycoplasma pneumoniae* IgM antibody test.

Abbreviations: IQR, interquartile range

eFigure 3A. Change Over Time in Empiric Antibiotic Agents, N=41 Hospitals, 6,553 Patients

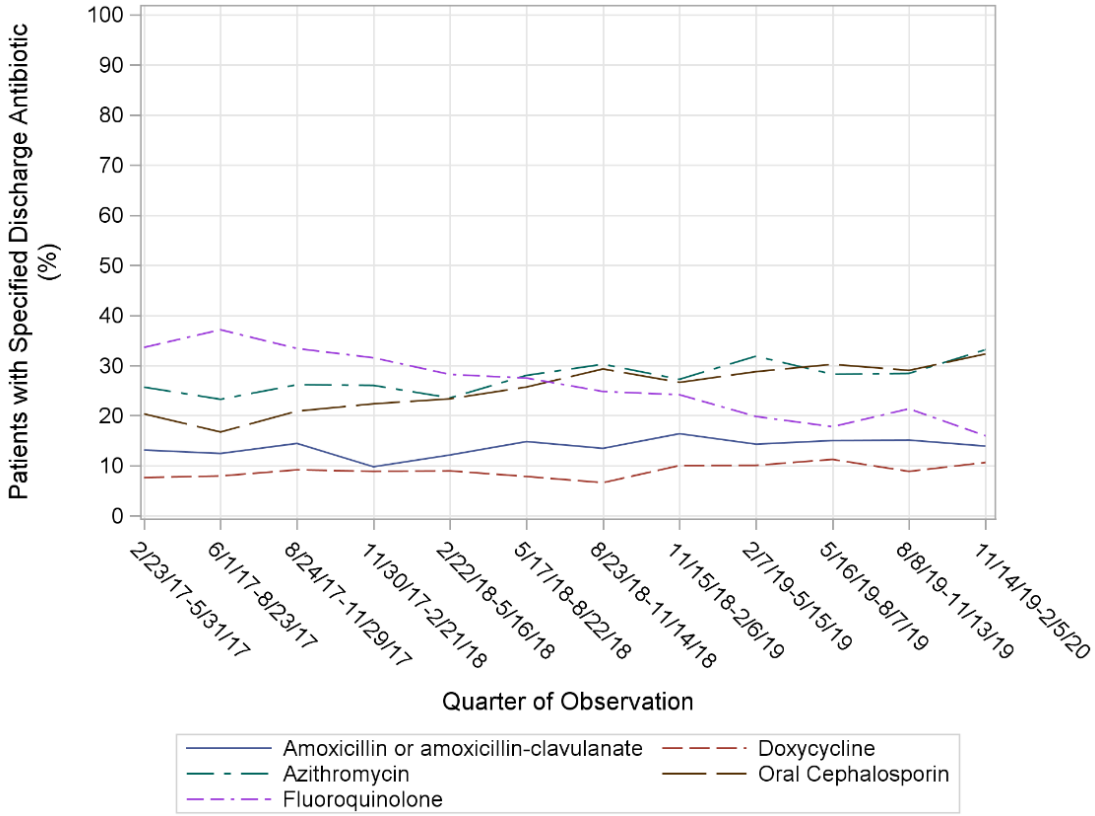


Legend: Graph shows change over time in the percentage of patients prescribed each antibiotic class on day 1 or 2 of hospitalization. Patients may receive antibiotics from multiple classes and therefore numbers may add up to more than 100%. Not all antibiotic classes included.

Antipseudomonal beta lactams refer to cefepime, piperacillin-tazobactam, aztreonam, ceftazidime, and meropenem.

Fluoroquinolones include levofloxacin, moxifloxacin, and ciprofloxacin.

eFigure 3B. Change Over Time in Discharge Antibiotic Agents, N=41 Hospitals, 6,553 Patients



Legend: Graph shows change over time in the percentage of patients prescribed each antibiotic class at discharge. Patients may receive antibiotics from multiple classes and therefore numbers may add up to more than 100%. Not all antibiotic classes included.

eTable 3. Association of Hospital Characteristics with Intercept and Slope of Improvement in Appropriate 5-day Antibiotic Treatment

Hospital Characteristic	Interaction Effect with Intercept	Interaction Effect with Slope
Academic Hospital	1.72 (1.01-2.94)	0.98 (0.92-1.05)
Profit Type		
Non-profit	REF	REF
For profit	1.07 (0.49-2.35)	0.92 (0.84-1.01)
Bed Size	1.09 (1.002-1.19)	1.00 (0.98-1.01)
Number of Hospitalists	1.01 (0.999-1.02)	1.00 (0.999-1.00)
System		
None	0.69 (0.35-1.38)	0.99 (0.91-1.09)
State	REF	REF
National	0.57 (0.33-1.01)	0.99 (0.92-1.06)

Hospital characteristics associated with appropriate 5-day treatment are shown. P-value were calculated from chi-squared tests with $P<0.05$ considered significant. Abbreviations: SD-standard deviation; ASP, antimicrobial stewardship program

[a] Academic hospital status from the American Medical Association's Fellowship and Residency Electronic Interactive Database Institution Directory.

[b] Profit status obtained from data.medicare.gov.

[c] Hospital bed size was obtained from the 2015 Michigan Certificate of Need Annual Survey.

[d] For participating hospitals, data are self-reported from the November 2019 hospital survey. For non-participants, data were collected from hospital websites.

[e] Refers to whether hospital belongs to a large healthcare system. Data obtained from the Michigan Health and Hospital Association Systems Listing (https://www.mha.org/About/Our-Hospitals/Michigan-Hospitals-By-Health-System).

eTable 4. Clinician-Documented and Patient-Reported Antibiotic- Associated Adverse Events, N=41 Hospitals

	Provider-Documented Adverse Events N=6,319 patients		Patient-Reported Adverse Events N=2,967 patients	
Outcome	Appropriate Duration N=2,155, n (%)	Excess Duration N=4,164, n (%)	Appropriate Duration N=783, n (%)	Excess Duration N=2,184, n (%)
Rash (not otherwise specified)	9 (0.42%)	23 (0.55%)	0 (0%)	11 (0.5%)
Diarrhea	6 (0.3%)	10 (0.2%)	8 (1.0%)	39 (1.8%)
Itching	4 (0.2%)	12 (0.3%)	0 (0%)	1 (0.05%)
Gastrointestinal Distress	4 (0.2%)	9 (0.2%)	5 (0.6%)	16 (0.7%)
Hives	3 (0.1%)	5 (0.1%)	1 (0.1%)	0 (0%)
Mucosal (Vaginal or Oral) Candidiasis	3 (0.14%)	3 (0.07%)	5 (0.6%)	7 (0.3%)
Neurologic (e.g., mental status changes, headache)	2 (0.09%)	3 (0.07%)	1 (0.1%)	2 (0.1%)
QT Prolongation or Cardiac Arrhythmia	3 (0.14%)	2 (0.05%)	0 (0%)	0 (0%)
Trouble Breathing	2 (0.09%)	2 (0.05%)	0 (0%)	1 (0.05%)
Intravenous Catheter Site Reaction	1 (0.05%)	2 (0.05%)	0 (0%)	0 (0%)
Liver Abnormalities	0 (0%)	3 (0.07%)	0 (0%)	1 (0.05%)
Angioedema or Facial Swelling	0 (0%)	2 (0.05%)	0 (0%)	1 (0.05%)
Myalgias or Musculoskeletal Complains	0 (0%)	1 (0.02%)	1 (0.1%)	1 (0.05%)
Anaphylaxis	0 (0%)	2 (0.05%)	0 (0%)	0 (0%)
Tendonitis	0 (0%)	1 (0.02%)	0 (0%)	0 (0%)
Fever	0 (0%)	1 (0.02%)	0 (0%)	0 (0%)
Renal Failure	0 (0%)	1 (0.02%)	0 (0%)	0 (0%)
Other	2 (0.09%)	1 (0.02%)	2 (0.3%)	1 (0.05%)

The number of patients who experienced/reported each adverse event is shown by category. Patients may have more than one adverse event. Patients were considered to have an excess duration if they received >6 days of antibiotic therapy and an appropriate duration if they received 5±1 days. Patient-reported adverse events were obtained via 30-day follow-up phone call. Of the 5,134 patients contacted to ascertain patient-reported adverse events, 2,967 (57.8%) responded.