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PROJECT STEP IN:

STEWARDSHIP THROUGH EDUICATION OF PROVIDERS  
IN THE INPATIENT SETTING

Implementation Guide to Establish Antimicrobial Stewardship  
Practices among Hospitalists and Other Hospitalist Clinicians

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Antibiotic overuse is one of the most pressing issues facing healthcare in the United States. In September 2014, a series of outbreaks of multi-drug resistant bacteria prompted President Obama to issue Executive Order 13676. The order commissioned a task force to evaluate and combat antibiotic-resistant bacteria. The resulting “Report to the President on Combating Antibiotic Resistance” concluded that “without rapid and coordinated action, the Nation risks losing the tremendous public health progress made over the last century from the discovery and development of antibiotic drugs, thereby threatening patient care, economic growth, public health, agriculture, economic security, and national security.”<sup>1</sup> The Centers for Disease Control and Prevention (CDC) estimates that antibiotic-resistant infections account for \$20 billion to \$35 billion in direct healthcare costs, 8 million additional days in hospitals and 23,000 deaths. In addition, *Clostridium difficile* (*C. difficile*), a downstream effect of antibiotic use, is responsible for 250,000 infections and 14,000 deaths.<sup>2</sup>

**The CDC, the Presidential Council of Advisors on Science and Technology, the Centers for Medicare & Medicaid Services (CMS), the National Quality Forum and The Joint Commission** have all identified antibiotic stewardship in healthcare as a critical measure to stem the tide of antibiotic resistance. The CDC has outlined core elements for antimicrobial stewardship programs (ASPs) for hospitals<sup>3</sup> that form the basis for The Joint Commission’s “Standard for Antimicrobial Stewardship”, which goes into effect January of 2017. This standard requires that all acute care hospitals and long-term care facilities have an ASP in order to maintain Joint Commission (TJC) accreditation and Medicare participation.<sup>4</sup>

**Inpatient antibiotic prescribing is under intense scrutiny.** Large-scale studies of inpatient antibiotic prescribing have found that up to **60 percent of inpatients receive antibiotics<sup>5,6</sup> and that nearly 50 percent of these antibiotics are unnecessary,**<sup>7,8</sup> with more than half of patients lacking microbiological documentation of infection, and 30 percent of patients lacking fever or leukocytosis.<sup>9</sup> Variability in antibiotic utilization among hospitals has been studied, allowing benchmarking and comparisons between facilities.<sup>10,11</sup> The Center for Medicare and Medicaid Services has proposed making antibiotic stewardship programs a requirement for all hospitals as part of new Conditions of Participation in Medicare. Now is the time for each hospital to take a critical look at the appropriateness of antibiotic use for its inpatients.

**Hospitalists prescribe a massive quantity of antibiotics, and thus are positioned to have an incredible impact on antibiotic use nationwide.** Hospitalists now care for 32 percent of all Medicare admissions,<sup>12</sup> and many of the top reasons for admission are due to infectious diseases. In 2009, pneumonia, septicemia and chronic obstructive pulmonary disease (COPD) exacerbations were in the top 10 principal diagnoses for admission, while skin and soft tissue infections grew by 176 percent among the uninsured compared to 1997.<sup>13</sup> The top areas of antibiotic use and overuse in inpatients include pulmonary, urinary and skin infections,<sup>8,14</sup> which are the bread and butter of hospital medicine. While the intensive care unit (ICU) utilizes a high density of antibiotics per patient, aggregate antibiotic use on the floors far exceeds the ICU given the larger numbers of patients.<sup>5</sup>

**The benefits of reducing inappropriate antibiotic use through stewardship have been demonstrated in hundreds of studies,** making antibiotic stewardship a win-win for patient care and hospital utilization. Antimicrobial stewardship programs have been shown to improve patient safety by decreasing the incidence of *C. difficile* infection (CDI)<sup>15</sup> and adverse drug events,<sup>16</sup> reducing readmissions and length of stay,<sup>17-19</sup> and reducing treatment failures. While most of these gains have been observed by traditional full-fledged stewardship programs, hospitalist-led projects are making their way into the stewardship mainstream in reducing treatment of asymptomatic bacteriuria,<sup>20,21</sup> identifying gaps in guideline-concordant therapy for healthcare-associated pneumonia (HCAP),<sup>22</sup> improving treatment of pneumonia, antibiotic use in cellulitis, and appropriate antibiotic use in the hospital and emergency department (ED).<sup>23,24</sup>

## Why Project STEP IN?

### *Hospitalists are in a strategic position to be stewardship leaders at this exciting time.*

In recent years, healthcare leaders have begun to understand that the breadth and scope of the antibiotic overuse epidemic necessitates a **new paradigm for antibiotic stewardship action**. Whereas the “traditional model” for antibiotic stewardship relied heavily on Infectious Disease (ID) specialists and ID-trained pharmacists,<sup>25</sup> who are sparse in number in many settings, the new model looks to front-line practitioners of every field as potential stewards of antibiotics<sup>26-28</sup> (Table 1, Figure 1). Taking lessons learned from the successes of infection control, i.e., the importance of hand hygiene, stewardship teams should emphasize that appropriate antibiotic use is everyone’s responsibility.

**Hospitalists have been identified as potential strategic leaders in antimicrobial stewardship due to the excellent alignment of hospitalist skills and values with stewardship principles.** Hospitalists are patient safety advocates, often engaging in care improvement initiatives, and thus have the requisite skills to lead process improvement projects.<sup>27</sup> Second, the benefits of stewardship, including potentially reducing length of stay and avoiding adverse events, are in line with hospitalist goals to deliver quality care without excess utilization.<sup>27</sup> Third, hospitalists are leaders in hospital quality and safety and often have access to data sources that can demonstrate the impact of stewardship initiatives.

Possible roles for hospitalists in antimicrobial stewardship include:

- **Members of the existing Antimicrobial Stewardship team**, giving feedback about feasibility and potential impact of interventions, educational programs and guideline updates
- **Peer educators** regarding appropriate antibiotic use and documented best practices
- **Innovators and implementers of hospitalist-driven stewardship interventions** (focus of Project STEP-IN)
- **Consultants** for stewardship programs seeking to develop technology and guidelines for hospitalist use
- **Researchers** in stewardship, investigating inpatient antibiotic use prescribing patterns, prescriber variation, behavior modification strategies and patient impact
- **Leaders of stewardship programs** in hospitals without access to an ID stewardship team leader (working closely with off-site ID consultation)

In hospitals that currently lack a structured stewardship program (34 percent of hospitals in a recent survey by the Society of Hospital Medicine (SHM)), Project STEP IN can be a great first step toward establishing an ASP under hospitalist leadership, with off-site ID consultation, or enhancing an already existing program led by ID or pharmacy leaders.

Project STEP IN aims to equip hospitalists with the ability to design and implement an antimicrobial stewardship intervention using evidence-based strategies for hospital medicine. The STEP IN stewardship project aims to modify local prescribing habits by first building a strong foundation of provider knowledge in antibiotic prescribing via four

online modules on antibiotic use in inpatients, and then constructing on that foundation an institution-specific process change that corrects one, or more, aspect(s) of local overuse.

The goal of the STEP IN program is not to train hospitalists to function as ID experts, but rather to harvest the low-hanging fruit of known pitfalls of antibiotic prescribing common to hospitalist medicine. The program can be implemented in a range of practice settings, and is customizable based on the resources of the facility. While not all facilities can develop a top-notch stewardship program overnight, all facilities can incrementally improve their antibiotic use with planning, effort and persistence.

The Society of Hospital Medicine hopes you will find this *Implementation Guide* and included tools useful as you aim to improve antibiotic use in your hospital. SHM is dedicated to the continuous improvement of the products and services offered. SHM encourages and welcomes feedback via email to [thecenter@hospitalmedicine.org](mailto:thecenter@hospitalmedicine.org).

Table 1. Annual Estimates of Antibiotic Courses and Active Hospitalists Versus Infectious Disease Specialists.

	National annual estimates, USA	Source
Hospital admissions	35,000,000	Hospital Association Fast Facts 2015 <sup>13</sup>
Inpatient antibiotic courses	17,500,000	Extrapolated from Magill 2014 <sup>5</sup>
Active hospitalists	44,000	Society of Hospital Medicine website <sup>29</sup>
Active ID specialists	6,154	AAMC Physician Specialty Databook 2014 <sup>30</sup>

Figure 1. Ratio of Antibiotic Courses to Hospitalists and ID Providers.  
(Derived from Table 1 sources.)



## How to Use the Guide to Implement Project STEP IN

Congratulations on your commitment to improving antibiotic use in your hospital!

The purpose of this *Guide* is to equip a hospitalist stewardship champion and the assembled multidisciplinary team to design and implement a focused intervention to improve antimicrobial prescribing in their hospital. **This Guide is NOT intended to be a comprehensive guide to building an Antimicrobial Stewardship Program (ASP)** as that is beyond the scope of this project, and has been covered extensively by the CDC,<sup>3</sup> the National Quality Forum,<sup>31</sup> The Joint Commission<sup>32</sup> and the Greater New York Hospital Association.<sup>33</sup> Instead, this *Guide* will focus on antimicrobial stewardship strategies that have been used successfully by hospitalists around the country.

The intervention categories that will be presented include three areas of stewardship interventions recommended in the CDC/IHI “Antimicrobial Stewardship Driver Diagram and Change Package” that have been shown to be feasible for hospitalist groups based on pilot testing in a variety of hospital settings. These intervention types include:

- 1) documentation of antibiotic indication and duration,
- 2) ensuring appropriate length of treatment based on evidence and
- 3) antibiotic time-outs to facilitate de-escalation of therapy.

We recognize that each institution is unique in terms of its experience conducting process improvement initiatives, available resources, and existing infrastructure for data collection and antibiotic ordering. Therefore, we will present sample interventions with the expectation that they will be adapted to facilitate their integration into daily practices at your institution. Having said that, within Section III we have outlined the “core” elements we believe are essential components of a STEP IN intervention.

The appendix provides tools for needs assessment, planning your intervention and managing the overall process. It also provides antibiotic references, treatment algorithms, sample order sets and an annotated bibliography. Additional references, resources and expert discussion forums are available online within the STEP IN Resource Room found at [www.hospitalmedicine.org/ABX](http://www.hospitalmedicine.org/ABX).

Project STEP IN and this *Guide* assume that each site will have unique informational needs. For this reason, information has been designed so you can follow a clear linear path to work through it, or skip around as needed. (Refer to the Table of Contents.) Sections I and II review key principles applicable to any quality improvement initiative such as gaining support for an intervention, creating a team and defining key outcomes.

Section III reviews the STEP IN intervention key components and suggests methods to adapt and launch the intervention at your institution.

Section IV of the *Guide* provides an evaluation plan, and Section V provides methods/approaches to maintain your improvements.





Look for this icon to identify worksheets that facilitate team-planning efforts.



Look for this icon at the end of each section for a summary of resources mentioned within the section and URLs. A complete listing of all websites mentioned throughout the *Guide* is also provided in Appendix A.

## Project STEP IN: Sample Project Plan

### *Stewardship through Education of Providers in the INpatient Setting*

The broad goal of Project STEP IN is to help you design and implement a **hospitalist-led, facility-specific** intervention to **improve antibiotic prescribing** (to “optimize the selection, dosing, and duration of antimicrobial therapy in individual patients”) in one, or more, of the following common hospital syndromes: urinary tract infection (UTI), pneumonia (CAP/HAP), skin and soft tissue infection (SSTI) and *Staphylococcus aureus* infections. The objectives for all stewardship interventions and programs are to achieve **measurable improvements** in microbial outcomes (antibiotic resistance), clinical outcomes (adverse drug events and CDI, morbidity and mortality), and healthcare costs (length of stay, pharmacy expenditures) through optimal antimicrobial prescribing.<sup>34</sup>

While all STEP IN sites will be working to improve antibiotic use using a specific set of interventions, each experience of implementing STEP IN will be unique. The practice culture at your institution, characteristics and availability of key team members, fiscal climate and other site-specific variables will influence who will be involved in your project, how those people interact and in which forums, how work gets done and the order in which some tasks are undertaken.

However, there are some common steps along the way that most, if not all, STEP IN teams will take. Certain tasks will have to be completed; certain stakeholders will have to be engaged, no matter the institutional culture or core team composition. The list of project tasks is meant to serve only as a general framework for your project. Details of the steps involved in the tasks are addressed throughout the STEP IN *Implementation Guide*.

## Sample Project Plan:

### *Planning Phase (Months 1-3)*

1. Conduct a **preliminary needs assessment** of your institution to determine current potential for a financial return on investment (ROI) for a stewardship intervention.
2. **Secure institutional support** for the initiative: engage senior leaders, secure needed resources.
3. **Assemble a multidisciplinary team** that is focused on analyzing and improving antibiotic use. Pharmacy, ID specialists and information technologists are central to most interventions.
4. **Equip a hospitalist leader(s)** to be a “Stewardship Champion” via provider education modules on antibiotic use in the target infections as well as stewardship principles.
5. **Conduct an in-depth institutional assessment.**
  - a. **Assemble baseline data on stewardship metrics** (i.e., measures of antibiotic use, or *C. difficile* rates, by provider group or unit if possible, obtain updated facility antibiogram) in order to identify targets for reductions in antibiotic prescribing.
  - b. **Assemble baseline data on provider knowledge** regarding treatment of the target infections.
  - c. **Analyze current workflows and/or knowledge gaps** that may be contributing to antibiotic overuse (prescribing inertia, gaps in documentation, provider turnover, etc.).
6. **Develop specific aims for reducing antibiotic use** for the target infection(s) that are time defined, measurable and achievable.

### *Implementation Phase Activities (Months 4-6)*

1. **Design a provider-centered stewardship intervention** to support one or more good habits of antibiotic prescribing highlighted in the educational modules.
2. **Develop policies, procedures, forms or other tools** needed for implementation of the intervention.
3. **Set a Go-Live date** by which the above policies will be in place in the target provider areas.
4. **Engage in staff education/outreach** to ensure that all stakeholders are aware of your efforts and, as appropriate, have an opportunity to offer input.

5. **Develop a provider education plan timeline** for all target providers to complete the “Hospital Infections 101” modules prior to the intervention “Go-Live.”
6. **Identify metrics and an evaluation strategy** that address the needs of your various stakeholders. Who will need to know what about your work, when will they need to have this information and what format will be most useful to them (process measures, outcome measures)?
  - a. Identify feasible stewardship metrics for your facility.
  - b. Identify financial metrics for your facility.
  - c. Plan for evaluation of provider knowledge after completion of educational modules.
7. **Implement a focused syndrome-specific or process-specific intervention** in the target provider area/unit.

### ***Intervention Phase Activities (Months 7-9)***

1. **Monitor functioning of each core element** of the ASP following implementation.
2. **Collect process measures on provider use of/adherence** to the intervention tool or pathway.
3. **Reassess your evaluation plan:** verify that data identified in your evaluation plan are being collected and appropriately capture the quality and quantity of your work.
4. **Keep stakeholders apprised of your progress.**

### ***Project Surveillance and Management (Months 4-12, and beyond)***

1. **Analyze data** to assess project performance.
2. **Adjust interventions.**
3. **Report data** to key stakeholders.
4. Continue to **monitor, improve and report** on your activities.



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## Overview of Program Essentials

Essential elements for improving antibiotic use include:

- **Institutional support** for and prioritization of this initiative, expressed as a meaningful investment in time, equipment, informatics and personnel. Ideally, a member of the C-suite should sign on as a sponsor and champion of the project.
- A **multidisciplinary team** or steering committee that is focused on improving antibiotic use in your institution.
- **Engagement of clinicians** and ancillary staff in the planning process.
- **Data collection and reliable metrics** (see Section II, Assessment Item 3). These data should be transformed into reports that inform the team and front-line workers of progress and problem areas to address.
- **Specific aims, or goals**, that are time defined, measurable and achievable.
- **Well-defined intervention protocols** (order sets, pathways, antibiotic time-out tools, etc.), with contingency plans, responsible personnel and provider support.
- **Policies and procedures** that are institution-specific and that support the intervention and promote its effective use.
- A **provider education strategy** to inform correct antibiotic use for your target infection.



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## **Section I:** Essential First Steps in Quality Improvement





## 1. Conducting a Preliminary Needs Assessment

Before you seek institutional support for your stewardship intervention, take a few days to weeks to conduct a brief survey of areas of antibiotic overuse at your facility. Ask frequently of service providers about which infections they see most often, which guidelines with which they are most/least familiar, if *C. difficile* is a big issue, or if multi-drug resistant gram-negatives are a significant concern. You will do an in-depth institutional assessment later on in the process, and you can always change your focus later. The purpose of this brief look is to generate a preliminary return on investment estimate for your hospital administration.

- 1) Read through Section II of this *Guide* and think about the prescribing practices among your hospitalist group.
- 2) Identify one antibiotic or disease process that you know is a glaring problem at your institution. Choose an area where data are relatively easy to obtain (i.e., without chart reviews).
- 3) Estimate the cost of overuse in this area.
- 4) Hypothesize a 10 to 30 percent drop in overuse after your intervention.
- 5) Use this cost savings as a conservative estimate of the impact of a potential stewardship intervention.

### Keep in mind:

- You can change direction if later on your in-depth assessment turns up a problem that has a larger potential impact. This is a “rough sketch” of the scale of the problem at your institution.
- The biggest cost savings are realized in year one, and the return on investment falls off after that. However, studies have shown that if changes are not sustained by institutional investment, the costs rapidly bounce back to pre-intervention levels.

Appendix B: Sample Analyses for Projected Cost Savings Based on Intervention Type, provides assumptions and estimates from the literature that can fill in gaps where facility-specific data are not available.

## 2. Obtaining Institutional Support

Substantial support is critical to the success of an ongoing stewardship initiative. The CDC and National Quality Forum place institutional support at the top of the list of the core elements of a facility stewardship program. Since this project is time-limited and not as comprehensive as a full Antimicrobial Stewardship Program (ASP), institutional support could take the form of a one-time grant or disbursement, rather than a standing budget item. The critical support needed to complete this project will be protected time for the team leader(s), but additional resources need to be requested based on the complexity of the planned intervention. Considering the above-mentioned developments in the political and regulatory climate surrounding antimicrobial stewardship, the value and relevance of stewardship activities and intervention should be readily apparent to hospital administrators. Failure to support stewardship activities is no longer an option, now that the Joint Commission standard is a reality.

To obtain support, you will need to clearly explain how your efforts may enhance quality and safety, improve processes and patient satisfaction, and impact the hospital's bottom line. A direct communication line to a senior administrative officer related to your effort should be in place before you go any farther, either by a direct reporting structure or by involving a senior administrator on the team. One example of an approach is to have an "executive sponsor" (e.g., CEO, CMO, CNO) or administrative champion of the project. This sponsor should receive regular updates on the project, or ideally attend committee meetings, and be an advocate of the project to the hospital leadership.

A sample letter you may want to send to a possible program champion is included in Appendix C. An executive sponsor is invaluable in helping your team focus on critical issues. However, it is equally important that your team understand where it fits in the overall quality improvement structure and priority of your organization. Frequently teams are assembled during a crisis, but need a plan that keeps them connected so that improvements that are made are sustainable and regularly reviewed. It is useful to ask your executive sponsor to whom or what structure your team reports, and reviews progress and outlines barriers.

Numerous studies showing the cost effectiveness of antimicrobial stewardship interventions in all healthcare settings make the business case for stewardship compelling in theory. Studies consistently show that an ASP can save a hospital \$200,000 to \$900,000/year in drug costs and *C. difficile* prevention depending on the type of interventions employed and the size of the hospital.<sup>15,35-37</sup> Stewardship interventions have also been shown to decrease hospital length of stay and infection-related mortality.<sup>38,39</sup> In addition, the data have shown that high-impact programs require dedicated personnel time and funding (Table 13 in Davey et al., 2013).<sup>40</sup> While these data exist, administrators often want to see local need prior to supporting a full team long term. A benefit of performing a STEP IN intervention is that your team will be generating baseline and post-intervention hospital-specific data about antibiotic use and cost-savings opportunities. Using STEP IN as a "pilot project," if successful, will provide your team with a stronger business case for supporting a robust and ongoing ASP, if one does not already exist in your hospital.

### 3. Stakeholder Reporting and Approval Process

A stakeholder is a person whose perspective and/or role is critical to a process. Antibiotic prescribing, dispensing and de-escalation involves many stakeholders, and it is important to ensure they or their representatives are on your team. **Engagement of front-line prescribers is the key to any successful stewardship intervention**, so including these prescribers as leaders on the team is critical. In addition, you should identify existing teams in the hospital that may already be working to improve antibiotic use and determine how to link or build on existing efforts. If your hospital has access to Infectious Disease (ID) specialists, these individuals should be invited to participate as well, as they may be able to guide the creation of protocols with institution-specific treatment advice.

At a minimum, you should include the following individuals with roles described in bold on your core team:

- **Hospitalists and hospitalist clinicians**
- **Leadership of clinical divisions** that will be impacted by hospitalist prescribing (i.e. Surgery if co-management is common)
- **Clinical pharmacists**
- **Infectious disease specialists (on-site or remote)**
  - Clinical microbiologists/lab staff
  - Clinical nursing staff
  - EMR builder
  - EMR data extraction expert
- **Data analyst**
  - Hospital epidemiologist
  - Emergency department staff
  - Patients
- Senior administrators, office of the Chief Financial Officer (CFO)/Chief Operating Officer (CEO)/Chief Operating Officer (COO)
- Quality improvement staff/utilization review analysts

Each hospital team must determine the skills and team members essential to the development and implementation of a feasible stewardship intervention given the current patterns of prescribing.

Given the complexities involved in antibiotic prescribing at most hospitals, intervention teams need people at all levels of the organization to help assess the problem, think creatively about process solutions and implement systemic changes through a consistent effort.



Appendix D provides a sample form to help you 1) identify key stakeholders, committees and special groups and 2) clarify the reporting structure and approval process for your interventions and resources needed.

### 4. Pulling the Team Together

In many cases, improvement activities are initiated by a few individuals who identify a big gap between the current and the best-known practices and then recruit others to their improvement team.

**TEAM LEADER(S):** Team leaders often include both a physician and a non-physician. For an antibiotic stewardship intervention, a respected hospitalist with leadership experience and a thorough knowledge of the prescribing culture at the institution is ideal. The leader is responsible for calling meetings and communicating directly with administrative and appropriate medical staff committees. The team leader does not need to be a content expert in antibiotic use, as he or she will receive education as part of Project STEP IN, but should be familiar with the relevant issues at the institution. The team leader needs to have the commitment and perseverance to drive the entire process forward. The team leader should become familiar with the basics of antimicrobial stewardship processes, methodologies and success stories (see Appendix E: Content Expert Annotated Bibliography on page 54).

**CONTENT EXPERTS:** A successful team needs access to an ID physician who is able to assist and advise in the process of adapting national guidelines into local guidelines based on hospital epidemiology and bacterial resistance patterns. Appropriate use of antibiotics for treatment of common infections is within the purview of every hospitalist, so while helpful, presence of an ID expert on the team is not essential day to day once the intervention is off the ground. However, ID expertise is needed during the design phase to ensure that proposed guidelines are safe and effective. The content expert should review and summarize the relevant literature, including its applicability to your institution and patient population.

**TECHNOLOGY AND DATA EXPERTS:** At all stages of the project, the team will need access to local data in order to identify targets for improvement and to monitor success. These people should be engaged in the project planning from the beginning, so that realistic analysis plans can be constructed.

Personnel who usually have access to institutional data on metrics of antibiotic use include:

- Hospital epidemiologists (*C. difficile* rates, incidence figures on hospital-acquired drug-resistant infections)
- Microbiologists (facility drug resistance rates/antibiograms)
- Quality assurance personnel (access to patient days, readmission rates, length of stay, mortality, core measure performance, *C. difficile* rates, hospital-acquired infection (HAI) rates)
- Financial analysts (access to patient days, length of stay)
- Pharmacy management (access to antibiotic costs/utilization)

Information technologists are also critical to integrating stewardship protocols into existing workflow, by modifying documentation templates and ordering screens in the electronic medical record, creating clinical decision support rules and implementing alerts to prescribers.

**TEAM FACILITATOR:** The team facilitator's main duties are 1) maintaining team rules, 2) helping the team leader stay on track by utilizing effective techniques for team and project management and 3) introducing the appropriate quality improvement (QI) tools for practical use by the team.

Mastery of QI tools at the onset of the project is not necessary. What is necessary is a willingness to learn QI tools and introduce them to the team as necessary. Mastery of stewardship literature is not as important for this position. Sometimes one person can be both team facilitator and team leader, but for more ambitious projects or for projects involving buy-in from disparate physician and nursing groups, a separate facilitator is very strongly recommended.



See Appendix F: Tools for Running an Effective Meeting on page 61.

**PROCESS OWNERS:** Participation of front-line personnel (e.g., nurses, pharmacists, hospitalists) is essential to having an effective team that succeeds in optimizing antibiotic use. Any intervention that targets antibiotic use among prescribers needs to receive buy-in from physicians and other prescribers in order to make lasting changes. The best hospitalist-driven antibiotic stewardship interventions come from the “bottom up” (i.e., workflow changes) not from the “top down” (i.e., formulary restrictions). The process owner should outline a strategy for peer-to-peer education and process modification that will allow the intervention to efficiently penetrate the hospitalist group.

See Appendix G: CDC Core Elements under “Key Support.”<sup>3</sup>

### 5. Antibiotic Stewardship Implementation Resources

Any team that wants to improve antibiotic use at its institution should understand the basics of antimicrobial stewardship processes, intervention types and measures of success. At least one or two hospitalists in your group should become very familiar with the general framework of stewardship improvements (i.e., CDC/IHI Antibiotic Stewardship Driver Diagram and Change Package, the GNYHA Antimicrobial Stewardship Toolkit, The Joint Commission Antimicrobial Stewardship Toolkit and the CDC Core Elements for Antimicrobial Stewardship Programs<sup>3</sup>). Other useful resources at your hospital may be individuals involved in previous QI projects, such as patient safety officers, QI leaders or QI facilitators. You should identify these individuals and learn from their expertise and experience if possible.

The Society of Hospital Medicine (SHM) also offers an array of training and technical support options for both physicians and non-physicians seeking to expand their knowledge and skills related to planning, implementing and evaluating quality improvement programs.

See:

Appendix G: CDC Core Elements for Antimicrobial Stewardship Programs

Appendix H: CDC/IHI Antibiotic Stewardship Driver Diagram and Change Package

Appendix I: Online Resources for Provider Education on Antibiotic Stewardship

### 6. Establishing Team Rules

At your very first team meeting, you should establish the team “rules,” and everyone needs to explicitly agree to them. It may even be useful to have all team members formally sign a document agreeing to these rules to communicate and stress their importance. The facilitator is usually given the task of gaining consensus on and enforcing the team rules.

Use the team rules in Appendix F on page 59 as a starting point. The team should modify the rules as needed and then officially record and acknowledge them. To some, these rules may appear a bit preachy. However, our experience is that breakdowns commonly occur when these basic rules are ignored or violated.

#### KEY PRINCIPLE

Everyone on the team must be encouraged to speak up, and his or her views must be respected. Traditional concepts of rank have to go “out the window.” A unit clerk should feel comfortable telling the lead physician, “I don’t think that will work because of [reason]. Why don’t we consider trying it this way?” In addition to these rules, it should be made very clear that potential members should notify the leader quickly if they cannot devote the requisite time and effort so a suitable replacement can be found. Timely minutes, as well as a quick turnaround for comments and corrections, should be the rule.

### 7. Establishing General Aims and Scope

Establishing team-supported goals is essential for maintaining focus and motivating the team. Start by creating broad goals that generally define the purpose of your program.

The broad goals of your hospitalist stewardship intervention should align with the strategic goals of ASPs in general. Dr. Christopher Ohl has summarized the primary goals of ASP as follows<sup>34</sup>:

- prevent or slow the emergence of antimicrobial resistance
- optimize the selection, dosing and duration of antimicrobial therapy in individual patients
- reduce adverse drug events, including secondary infections (e.g., *Clostridium difficile* infection [CDI])
- reduce morbidity, mortality, length of hospitalization and healthcare-related costs

Stewardship programs accomplish these goals by “providing a **framework for accountability** in the use of antimicrobial agents and by improving, modifying, and decreasing such use at the level of the individual patient.”

General aims should fall into one of the above categories, and should ideally reflect an **alignment of the interests of the hospitalist group** and a clinically and/or financially significant problem of **strategic importance to the hospital administration**.

## Section I: Essential First Steps in Quality Improvement

Your team must now refine the general aims. To do this, you'll add an expectation of time to achieving the aim and define the inpatient subpopulation in question. Specific aims should follow the **SMART** Criteria: **S**pecific, **M**easurable, **A**chievable, **R**ealistic, **T**ime-related.

For example:

General aim 1: Substantially improve the rates of CDI in our hospital.

Is converted to Specific aim → In 1 year, the incidence of CDI per 1,000 patient days of hospitalization will decrease by 25%.

General aim 2: Decrease excess antibiotic use for cellulitis.

Is modified to Specific aim → By July of 2017, the number of patients receiving empiric vancomycin for non-purulent cellulitis will decrease by 30%.

General aim 3: Improve adherence to national guidelines for treatment of community-acquired pneumonia.

General aim 4: To reduce the mean duration of antibiotic therapy for uncomplicated CAP from 10 days to 5 days over one year.

General aim 5: To reduce the use of antibiotics in asymptomatic bacteriuria.

Is modified to specific aim → In 3 months, to educate all emergency room providers and hospitalists on the evidence-based indications for urine culture ordering.

As your team develops, your challenge will be to define many of the terms in your general aim, which will entail developing defined metrics and more mature, specific, time-defined aims. For example, what part of the antibiotic overuse do you want to approach first? Over-diagnosis, or overtreatment? Do you want to impact process measures (provider education), utilization measures or patient outcomes? What data do you have access to in able to measure success?



Use the worksheet in Appendix J on page 69 to record your general aims.

A “stretch” goal should be established that is aggressive enough to mandate a change in the design of your current process to achieve it.

You must also determine the target population(s) for improved outcomes and clearly define the scope of your efforts. Consider these questions:

- Where are the biggest misuses of antibiotics occurring?
- Will you target one ward or a service?
- Will you target one or more groups of physicians? House staff?
- Will you target non-medicine physicians, i.e., surgical services?
- How will you pilot your intervention and for how long?
- Which patient population(s) will be targeted?



It is advisable to start small (“one doc, one day”)<sup>41</sup> and spread your interventions to other areas after you have ensured that it is feasible and effective with a smaller group of providers.

Even if the scope of your effort may include all patients in your hospital or system, the interventions you choose should be piloted on a small scale when possible. The bottom line is this: Think BIG, but start small. Don’t bite off more than you can chew initially, but use serial testing and learning on a small scale to make even very large projects more manageable.

### 8. Going from General Aims to Specific Aims

General aim 1: Substantially improve the rates of CDI in our hospital.

Is converted to Specific aim → In 1 year, the incidence of CDI per 1,000 patient days of hospitalization will decrease by 25%.

General aim 2: Decrease excess antibiotic use for cellulitis.

Is modified to Specific aim → By July of 2017, the number of patients receiving empiric vancomycin for non-purulent cellulitis will decrease by 30%.

Progress toward core aims should be tracked, trended and publicly reported in run charts (see Section IV, Trending Data Over Time: Run Charts and Statistical Process Controls), with frequent reiteration of the ultimate goals. After you have collected baseline data, revisit general and specific aims you established (Appendix J) and for each one, create more specific aims. These aims should be reviewed and revised quarterly based on the progress of your intervention and what you learn to be achievable and realistic. Recall general aims from Section I: Establishing General Aims and Scope on page 9.

### 9. Financial Considerations

Implementation of the components of Project STEP IN may impact utilization of inpatient resources — either positively or negatively. Attending to the logistical issues outlined in the toolkit could help eliminate unnecessary pharmacy costs, adverse events and CDI, and potentially shorten length of stay. On the other hand, monitoring and intervening on daily antibiotic choices requires time and energy on the part of stewardship team members. Personnel time, data management needs, data analysis costs, marketing material costs and intervention-dependent expenses all increase resource utilization.

It is the responsibility of the clinical members of the team to articulate what you are trying to achieve (i.e., “reduce unnecessary antibiotic use”) and identify the patients you are targeting (i.e., “all patients admitted with a diagnosis of community-acquired pneumonia”). The team liaisons either from the CFO’s office or Utilization Review who have access to the utilization/cost and revenue information will want to analyze this data to understand the financial implications pertinent to the proposed project.

## Section I: Essential First Steps in Quality Improvement

Patient epidemiology, local bacterial resistance, current state of antimicrobial stewardship and local prescribing habits are four variables that will influence the financial consequences of your proposed project. If you are in a hospital that frequently admits elderly patients with delirium, who usually get diagnosed and treated for UTIs, then the impact of targeting asymptomatic bacteriuria could potentially lead to large cost savings in your facility.

If your facility has high rates of hospital-acquired *C. difficile* infections or hospital-acquired MRSA bacteremia, then your hospital will be subject to reduced Medicare payments starting in 2017 when the Centers for Medicare & Medicaid Services will add these two conditions to the Value Based Purchasing program. Hospitals are bound to lose payment for these conditions in 2017, similar to what is now in place for other preventable hospital-acquired conditions (<https://www.gpo.gov/fdsys/pkg/FR-2014-05-15/pdf/2014-10067.pdf> - page 28119). The higher your facility's baseline rates of *C. difficile*, the more you stand to gain from antimicrobial stewardship efforts. As mentioned above, an active antimicrobial stewardship program will likely be required as a condition of Medicare participation in the next five years. These important changes to Medicare reimbursement will provide strong financial incentives to your hospital to engage in antimicrobial stewardship projects.

The challenge of demonstrating the value of a stewardship intervention lies on the shoulders of the STEP IN team. Presenting the hospital leadership with pending changes in the regulatory environment in addition to projected facility-specific cost-savings data flowing from a stewardship intervention will build an excellent case for hospital support of a STEP IN intervention.

Additional resources can be found at:



<https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/HospitalAcqCond/HAC-Regulations-and-Notices.html>

[http://www.idsociety.org/Hospital\\_Acquired\\_Conditions/](http://www.idsociety.org/Hospital_Acquired_Conditions/)





**Fight**  
The  
**RESISTANCE**

## **Section II:** In-Depth Analysis of Current Processes and Opportunities for Improvement



### 1. Performing an Institutional Assessment of the State of Antimicrobial Stewardship

This section contains a series of important headings that may highlight key priority areas for your institution. You should first review the headings and determine whether these represent the critical priority areas related to antimicrobial stewardship in your hospital, and then review the accompanying questions. Use the questions as a starting point for dialogue and discussion. You may find that some questions are more central to your organization's antimicrobial stewardship issues than others. You may also find that there are additional questions your team wants to include. These headings and questions should be used as a starting point for your team's work related to understanding your current antimicrobial stewardship.

One of the first steps to improve antibiotic use is conducting a thorough survey of your current care environment, order sets, critical pathways and guidelines, and care processes central to antibiotic use. The following section provides a framework for such an assessment. The goal of these assessment questions is to help you identify the "low-hanging fruit" for areas of stewardship in your hospital, i.e., the areas, primarily among hospitalists, where there are clear patterns of antibiotic excess in conflict with best practices.

Before you begin analyzing your current areas for improvement, it might be helpful to know that **three infections are known to be sources of antibiotic over-prescribing in other studies and nationwide: urinary tract infections, pneumonia, and skin and soft tissue infections (SSTI)**. These areas have been designated as "low-hanging fruit" by stewardship leaders and are recommended target areas for improvement in facilities that have not undertaken extensive stewardship activities in the past. These three infections are the top infectious diagnoses treated in U.S. hospitals<sup>13</sup> and account for a large portion of antibiotic use.<sup>8,41,42</sup> Each of these diagnoses is associated with "prescriber pitfalls" that are potential targets for intervention, including treatment of colonized patients as if they were infected, excessive treatment durations and overly broad-spectrum antibiotic use. This section will recommend assessment strategies to determine which of these infections is the biggest problem at your hospital.

Note: You might find it helpful to use process mapping when you do your assessment of selected areas of interest. (See Section II, 2. Process Flow Mapping: A Critical QI Tool on page 26 for more information and examples.)

#### *Understanding the State of Antibiotic Use at Your Institution*

Each facility has its own set of assets and opportunities. Review the following grid to identify where your hospital rates as it applies to stewardship capacity and ongoing activity. **Strive to use Project STEP IN to build capacity and move your hospital into a more advanced category in one or more areas of the CDC Core Elements.**

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### Facility Capacity Grid

This table helps facilities categorize themselves into three different levels of stewardship capacity based on currently available resources. Each level is assumed to include the elements of the preceding level. This is a rough guide organized along the lines of the CDC Core Elements.

	Basic	Intermediate	Advanced
<b>Leadership Support</b>	None	Written support	Funding and reporting in place
<b>Accountability</b>	Physician OR Pharmacy Leader	Physician AND Pharmacy Leaders	Multidisciplinary stewardship team
	0 FTE	0.1 – 0.5 FTE MD 0.1 – 0.5 FTE Pharm	0.5 – 1.0 FTE MD 0.5 – 1.0 FTE Pharm
Available support	Infection Control	Nursing, Lab, Infection Control	Quality, Data Analysts
<b>Drug Expertise</b>	Staff Pharmacist	Clinical Specialist Pharmacist	ID/Stewardship Pharmacist
	Rare or no ID consultation available	ID consults on site with a stewardship emphasis	Subspecialty ID consultation services with dedicated stewardship ID physician
<b>Stewardship Actions</b>	Pharmacy dose adjustments, formulary restriction	Syndrome-specific guidelines, IV to PO conversion, documentation at point of care	Antibiotic time-outs, 48-hour review, targeted interventions
EMR capability	None	Provider alerts for dose adjustments	Order sets/provider alerts for clinical syndromes
<b>Tracking</b>			
Antibiotic data	Pharmacy data available – purchasing only. No EMR	Drug administration data available from EMR	Calculating DOT/1,000 patient days or DDD/1,000 patient days
Microbiology	No microbiology on site, regional antibiogram	On-site microbiology + Local antibiogram	On-site microbiology Rapid diagnostics/PCT testing Antibiogram by unit
Administrative data	Facility level readmissions, mortality	Readmissions and mortality by ICD code	Detailed outcome tracking of infectious syndromes
<b>Reporting</b>	<i>C. diff</i> rates MRSA rates	Facility-wide antibiotic use Drug resistance rates	Unit and provider-specific antibiotic use
<b>Education</b>	Fliers, posters	Intermittent educational talks, detailing sessions	Ongoing feedback and education to providers

# Section II: In-Depth Analysis of Current Processes and Opportunities for Improvement

## Assessment Item 1: Institutional Support for Stewardship

- Does your institution already have an intact Antimicrobial Stewardship Program (ASP) that is institutionally supported? If so, are personnel receiving support to dedicate time to stewardship? Is current support adequate or inadequate?
- What is the institutional buy-in (from administration), and do you understand how your team fits into the organization's clinical quality improvement structure and priorities? Is funding available for short-term quality improvement interventions apart from or within ASP funding?
- Do you have the resources available for forming a team and supporting its efforts in formulating order sets, protocols, educational programs and metrics to optimize antimicrobial use?

If you haven't already done so, Section I.2. Obtaining Institutional Support (page 5), will assist you in enrolling the administration in your cause and in defining the medical staff entities to whom your team needs to report.

## Assessment Item 2: Presence of a Multidisciplinary Stewardship Team

- If your institution has an ASP, have you engaged them as partners in the planning process for your project?
- What is the relationship of the local ID group to the hospitalist group? Are there ID consultants willing and able to help with the project?
- Have you formed a truly multidisciplinary team or steering committee that works on the front lines of healthcare delivery, as outlined in Section I.4. Pulling the Team Together (page 7)? If not, do so now! You will not be able to complete the assessment without the knowledge of representatives from a variety of disciplines. However, you also want to be mindful of not waiting for every area to be represented prior to initiating your process. You can always add team members and review membership along the way. The key is to engage and include the key multidisciplinary stakeholders.

## Assessment Item 3: Reliable Data Flow and Metrics

The CDC and the National Quality Forum (NQF) have suggested several metrics for successful stewardship programs. In its recent publication, *Antibiotic Stewardship in Acute Care: A Practical Playbook*,<sup>31</sup> the NQF outlines strategies for data collection according to available hospital resources (basic, intermediate and advanced). The NQF-endorsed antibiotic use measure that hospitals should strive to collect is the Standardized Antibiotic Administration Ratio (SAAR), which is similar to the Standardized Incidence Ratio (SIR) currently reported for *C. difficile*. The CDC and NQF encourage (and will later require) hospitals to report antibiotic use to the National Healthcare Safety Network (NHSN) using antibiotic days of therapy/1,000 patient days, along with the unit type within which the antibiotics were used. Any dose of a unique antibiotic given to a patient within a 24-hour period will count toward the antibiotic days. For instance, a patient receiving ceftriaxone and azithromycin will count as 2 antibiotic days/1 patient day. The NHSN will aggregate the national data, determine expected usage rates based on unit type and facility factors, and issue the facility an SAAR.



## Section II: In-Depth Analysis of Current Processes and Opportunities for Improvement

**Which of the following metrics are available or easily developed for your hospital?**

**Are the data communicated to the front-line prescribers, and if so, how?**

Here is the list of all the metrics suggested by NQF:

### Basic: Process Measures

- Adherence to documentation policies, e.g., requirement to document indications for antibiotic use and requirements to document performance of time-outs.
- Tracking of diagnosis, drug, dose, duration and de-escalation with antibiotic time-out.
- Adherence to facility-specific treatment recommendation or guidelines.
- Adherence to specified interventions. [i.e., not ordering culture for asymptomatic patients.]
- Accurate antibiotic allergy and adverse reaction histories.

### Intermediate: Outcome Measures

- Sequential tracking of antibiotic resistance patterns (e.g., gram-negative resistance).
- Tracking of *C. difficile* infection rates.
- 30-day readmission rates for pneumonia and *C. difficile*.
- Length of stay for community-acquired pneumonia, SSTI.
- Mortality for *Staphylococcus aureus* bacteremia, community-acquired pneumonia.

### Advanced: Antibiotic Use Measures

- Number of antibiotics administered to patients per day (i.e., days of therapy, or “DOT”). Hospitals can use the CDC National Healthcare Safety Network (NHSN) Antibiotic Use Option to track and benchmark days of therapy.
- Grams of antibiotics used (defined daily dose, or “DDD”) could be used if DOT not available.
- Standardized antibiotic administration ratio (SAAR), an NQF-endorsed quality benchmarking measure for antibiotic use, available to hospitals enrolled in the NHSN Antibiotic Use Option.
- Direct antibiotic expenditures (purchasing costs).

Help on data flow, formulating metrics and presenting data is available in Section III: STEP IN Interventions to Improve Antibiotic Use for Inpatients, on page 28.

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## Assessment Item 4: Current Stewardship Practices

Does your institution have any of the following CDC Core Elements for Antibiotic Stewardship in place already?<sup>3</sup>

### Policies to support optimal antibiotic use

- Policies for documentation of dose, duration and indication for every systemic antibiotic
- Facility-specific treatment recommendations for common infections (particularly UTI, cellulitis and pneumonia)

### Broad interventions to improve antibiotic use

- Antibiotic “time outs” — a systematic questionnaire, alert or form to prompt clinicians to discontinue unnecessary antibiotics at a set interval (48–72 hours) after antibiotics have started
- Prior authorization for restricted antibiotics
- Prospective audit and feedback — external reviews of antibiotic therapy by an expert to ensure that antibiotics are appropriate (triggered by drug formulary or infectious syndrome)

### Pharmacy-driven interventions

- Automatic IV to PO conversion
- Dose adjustment/optimization
- Automatic alerts for duplicate therapy
- Time-sensitive automatic stop orders
- Detection and prevention of antibiotic-related drug interactions

### Infection and syndrome specific interventions

- Community-acquired pneumonia
- Urinary tract infections
- Skin and soft tissue infections
- Empiric coverage of MRSA infections — de-escalation after 48 hours if no MRSA
- Clostridium difficile infections — stopping unnecessary antibiotics
- Treatment of culture proven invasive infections

## Section II: In-Depth Analysis of Current Processes and Opportunities for Improvement

### Assessment Item 5: Standardized Processes for Treatment of Common Infections

- What standardized processes for diagnosis and treatment of common infections already exist? (I.e., Does your facility have order sets or guidelines for sending and collecting urine or sputum cultures? For treatment of community-acquired pneumonia, cellulitis or UTI?)
- If standardized processes exist, what clinical groups or teams own the processes? (I.e., are there different UTI order sets for Medicine and the Emergency Department?)
- What elements of infection treatment can/should be standardized? (I.e., what are common infections that could have order panels or protocols for culture ordering, culture collection, imaging orders, antibiotic choice, ID consultation?)
- What elements of infection treatment need to be more customized to a specific patient population? Are there patients who should be excluded from treatment protocols (i.e., transplant patients, children, immunocompromised patients)?
- If you wanted to standardize treatment or culture ordering, what forums or platforms exist for standardization? Does your hospital have an EMR or paper-based system into which treatment algorithms could be integrated? Do all your hospitalists use a tablet or app?
- What are other clinical scenarios that may serve as successful models of standardization at your facility?

### Assessment Item 6: Identifying Specific Hospital Areas of Antibiotic Overuse

Using pharmacy data, quantify antibiotic use, if possible by unit/service, drug and diagnosis.

- Which treatment areas/units, infectious syndrome or individual providers stand out as above average in terms of antibiotic use? Look at the Emergency Department, Medical Units, Intensive Care Units and Surgical Floors.
- Is overall antibiotic use in your facility increasing or decreasing over time? Are increases occurring in a single unit or across the entire facility?
- Which antibiotics are most commonly prescribed, and for which syndromes are they being used? Note: may be able to use billing codes or do chart sampling to determine which infections are being targeted.

### Assessment Item 7: Learner/Target Audience Assessment

- What are the current characteristics of providers to be targeted by the stewardship intervention? What hours will they be available for education, and what is their background educational level/experience in the treatment of infections (i.e., NP/PA/MDs/nurses/day providers/nocturnists)?
- Are there other clinical services that will be impacted by hospitalist-driven interventions? (I.e., Does the hospitalist group admit to other services or do other services admit to the hospitalist group? Do hospitalists co-manage surgical patients?)
- What is the culture of your hospitalist group when it comes to standardization? Are providers welcoming of treatment algorithms?
- How often does the group meet?
- Which communication strategy best works for the group?

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### Assessment Item 8: Incidence of *Clostridium difficile* Infection (CDI)

If antibiotic use data is not readily available, CDI incidence could also be charted across the hospital to identify areas of potential antibiotic over-prescribing, though lapses in infection control may also explain high rates of CDI. In general, infection control practices should be optimized first, and then a facility can focus on the impact on antibiotic prescribing on CDI, but simultaneous interventions can be done in emergencies. Engage your Infection Control department for assistance with these questions.

- Is your hospital consistently exceeding the national SIR for CDI? (See state progress reports at <http://www.cdc.gov/hai/progress-report/index.html>.)
- Are effective infection control measures in place?
- How many cases of hospital-acquired CDI did your facility have over the past two years?
- What would be the financial impact of not getting reimbursed for those cases?

Prior to planning an intervention for CDI, attempt to get specific details and patterns of use for the antibiotics most highly associated with this infection: clindamycin, fluoroquinolones (especially moxifloxacin and ciprofloxacin), 2nd and 3rd generation cephalosporins.<sup>43-45</sup> Antibiotic prescribing patterns are best identified by working with Pharmacy to conduct a Drug Use Evaluation (DUE). See Appendix K for an example DUE form. More targeted questions would be:

- Which units use the most clindamycin and for what diagnoses?
- Which units use the most cefazolin and ceftriaxone and for what diagnoses?
- Which units use the most ciprofloxacin and moxifloxacin and for what diagnoses?

### Understanding Your Institution's Approach to the "Big 4" Infections

The following assessment items are recommended to obtain more specific baseline data for the most common inpatient infections at your institution. These **assessments will require a significant commitment of time and energy**, so engage as many team members as necessary and delegate tasks as needed. Perhaps choose one area you already know presents a problem at your institution to explore in more depth.

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### Assessment Item 9: Urinary Tract Infections (UTIs)

UTIs are the number one area of antibiotic overuse in hospitals and long-term care facilities.<sup>42,46</sup> Clear guidelines exist regarding the diagnosis and treatment of urinary infections,<sup>47,48</sup> and several studies have shown that algorithms and treatment guidelines governing the diagnosis and treatment of UTIs reduce unnecessary antibiotic use without compromising patient care.<sup>41,49</sup> These efforts make UTIs a great starting place for antibiotic stewardship interventions in many healthcare facilities.

Overuse of antibiotics in the area of urinary infections is due to both overdiagnosis and overtreatment. Common pitfalls along the clinical pathway include:

- 1) Treatment of asymptomatic bacteriuria (ASB) with antibiotics (i.e., sending urine cultures for nonspecific symptoms, treating positive urine cultures regardless of symptoms). See Appendix L for guidelines regarding which clinical symptoms differentiate ASB from UTI.<sup>20,46-49</sup>
- 2) Excessive treatment durations for diagnosed urinary infections.
- 3) Excessively broad-spectrum treatment of urinary infections.

Analyzing the current state of UTI treatment in your facility can start at the level of diagnosis and/or treatment. **Below are some suggested strategies to determine whether and how often UTIs are being overdiagnosed or overtreated in your facility.**

1. Diagnosis: Sample strategies for collecting baseline data on urine cultures (UCs) and urinalyses (UAs)
  - Ask the microbiology lab for a list of UAs and UCs ordered by hospitalists over the last three months. Review the charts of 20–40 cases to determine what percentage of cases lack guideline indications for urine cultures. Report as a percentage. For sample studies see Hartley<sup>20,46</sup> and Trautner.<sup>49</sup> Use the surveillance form provided (Appendix M).
  - Obtain a list of all UCs ordered at your facility over the past three to six months. Review the ordering providers and units to see where most of these orders are being generated. Can you think of clinical reasons why the orders cluster in one area? Are the emergency room providers ordering a majority of the cultures? Are urine cultures embedded inappropriately in an order set for “Altered Mental Status”? You may need to review 20–40 charts in each area to determine the indications for culture ordering. Report the number of UAs and UCs by unit. Report what percentage are appropriate based on guidelines as above. Use the surveillance form provided (Appendix M).
2. Treatment: Sample strategies for collecting baseline data on treatment of UTIs.
  - Obtain a list of all “first of admission” positive UCs from the microbiology lab. Review the charts of 20–40 cases to determine how many of these cases met criteria for UTI, and how many were asymptomatic, or did not have symptoms documented in the chart. Previous studies have shown that up to 60 percent of patients who receive antibiotics for a UTI do not meet evidence-based criteria for UTI.<sup>20</sup> Use the assessment form provided (Appendix M).

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- Obtain a list of patients discharged on ciprofloxacin for UTI, using billing codes (Appendix N). Review the charts to determine how many of these patients were treated with excess duration of antibiotics for cystitis or pyelonephritis. Use the assessment form provided (Appendix M).

### Assessment Item 10: Skin and Soft Tissue Infections (SSTI)/Cellulitis

Skin and soft tissue infections have been on the rise nationwide since the advent of community-acquired MRSA, both as a cause of ED visits and hospital admissions.<sup>13,50</sup> Skin and soft tissue infections are rife with antibiotic overuse for multiple reasons, but the following represent the “low-hanging fruit” for hospitalist-driven stewardship interventions: 1) providers prescribe antibiotics after abscess drainage when not indicated,<sup>51-53</sup> 2) many noninfectious mimics of cellulitis are treated with antibiotics,<sup>54,55</sup> 3) cases of uncomplicated non-purulent cellulitis are treated with anti-MRSA antibiotics despite evidence that this is not necessary<sup>56-59</sup> and may carry higher failure rates,<sup>60</sup> 4) duration of antibiotics is excessive despite evidence that shorter courses are effective<sup>61,62</sup> and 5) gram-negative coverage is given in many cases, though it is only indicated in a very few instances.<sup>63</sup>

Analyzing the current state of SSTI treatment in your facility can start at the level of diagnosis or treatment. **Below are some suggested strategies to determine whether and how often SSTIs are being overdiagnosed or overtreated in your facility.**

1. Diagnosis: Sample strategies for collecting baseline data on over-diagnosis of cellulitis
  - Work with a Dermatology or ID consultant to prospectively evaluate 20 patients admitted for cellulitis. Document how many cases are diagnosed with an alternative non-infectious diagnosis by the consultant, and how many had antibiotics discontinued.
  - Obtain a list of patients with ICD-9/ICD-10 (Appendix N) principal discharge diagnoses of cellulitis or SSTI. Review 50 of these cases with an ID consultant to determine the composition of your cellulitis cases according to the criteria in Jenkins et al., 2010.<sup>60</sup> Alternatively, use the Treatment Algorithm (Appendix O) to determine whether patients received appropriate antibiotics. If the nonpurulent and abscess cases represent a large portion of your SSTI, your institution likely has a lot to gain from stewardship interventions in this area. Use the categorization form provided (Appendix P).
2. Treatment:
  - Obtain a list of patients with principal ICD-9/ICD-10 codes (Appendix N) for cellulitis or skin and soft tissue infections over the past year. Ask the pharmacy for antibiotic treatment data for these cases. Report the percentage of patients who received the following drugs: piperacillin/tazobactam, meropenem/imipenem, ertapenem, cefepime, ciprofloxacin. If 60–70 percent of patients received any one of these drugs, your institution has a lot to gain from stewardship in this area.
  - Using the list above that is categorized according to the Jenkins study, evaluate vancomycin use for each of the categories. The vancomycin use should be <5–10% for nonpurulent cellulitis.

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### Assessment Item 11: Community-acquired Pneumonia (CAP)

Pneumonia is the 8th leading cause of death in the United States<sup>64</sup> and a common cause of antibiotic overuse.<sup>8</sup> Similar to UTIs and SSTIs, the reasons for antibiotic overprescribing in pneumonia are due to 1) overdiagnosis (treating noninfectious syndromes, viral syndromes)<sup>65,66</sup> and 2) excessive antibiotic treatment (too broad of therapy, too long of a duration).<sup>67</sup> The IDSA Guidelines recommend a treatment duration of five days, with longer courses for people with complicated disease who do not respond to initial therapy,<sup>68</sup> though a randomized trial from Switzerland showed that even three days is sufficient for people who respond well.<sup>69</sup> In clinical practice, patients receive much longer than this, with a common median duration being 10–12 days<sup>70</sup> regardless of patient response.

Analyzing the current state of CAP treatment in your facility can start at the level of diagnosis or treatment. **Below are some suggested strategies to determine whether and how often CAP is being overdiagnosed or overtreated in your facility.**

1. Diagnosis:
  - Obtain a list of patients with a principal diagnosis of pneumonia discharged in the past month (ICD-9/ICD-10 – Appendix N). Manually review 30 charts from this list to determine what percentage met diagnostic criteria for definite CAP. Use the assessment form provided (Appendix Q).
  - Review 30 of the cases above to determine what percentage had the following diagnostic data performed: sputum cultures obtained, blood cultures obtained, urine antigen testing for *Streptococcus* and *Legionella*, procalcitonin levels obtained (Appendix Q).
  
2. Treatment:
  - Manually review 30 of the charts from the above patients using an assessment form for appropriate use of antibiotics for CAP (Appendix Q).
  - If possible, obtain pharmacy treatment data on each of these cases to determine which drugs were used most commonly and for how long. Calculate a median duration of antibiotics for all pneumonia cases. If it is >7 days, your institution likely has a lot to gain from interventions in this area. If the median duration of azithromycin is >3 days, this can also be improved.

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### Assessment Item 12: *Staphylococcus aureus* — MRSA

In the era of MRSA, clinicians have good reason to fear infection with this organism, and so empiric coverage is appropriate for many clinical syndromes according to the IDSA Guidelines (Appendix R). However, continued empiric coverage beyond 72 hours in the absence of positive cultures is a frequent cause of inappropriate vancomycin use. Overuse of vancomycin, even for short courses, is a cause of escalating vancomycin resistance in *Staphylococcus aureus*<sup>71,72</sup> and unnecessary nephrotoxicity.<sup>73,74</sup> Even in areas of high MRSA endemicity, vancomycin can be safely de-escalated according to HICPAC criteria.<sup>75</sup> In patients with pneumonia, the absence of MRSA on nasal and throat screening has an excellent negative predictive value for MRSA pneumonia in low prevalence settings.<sup>76</sup> The key to vancomycin de-escalation is to obtain cultures prior to antibiotics, though respiratory cultures remain positive for several days even after vancomycin initiation.<sup>77</sup> In addition, many physicians do not de-escalate to a beta-lactam for methicillin-susceptible *Staphylococcus aureus* (MSSA) when it is identified, despite the fact that vancomycin is associated with more clinical failures for MSSA, and that de-escalation for MSSA is a CMS quality measure reported for physicians.<sup>78</sup>

“Low-hanging fruit”: Areas of inappropriate use of vancomycin/daptomycin/linezolid in hospitalized patients:

- Continued empiric therapy for fever/leukocytosis when cultures are negative for MRSA
- Continued therapy when MSSA is identified
- Empiric treatment of mild to moderate non-purulent cellulitis
- Empiric treatment of CAP in the absence of severity or MRSA risk factors
- Continued use for HCAP beyond 72 hours in the absence of positive cultures

Analyzing the current state of vancomycin use in your facility can start at the level of diagnosis or treatment.

**Below are some suggested strategies to determine whether and how often vancomycin is being overused in your facility.**

#### 1. Diagnosis:

- **Under-culturing:** Obtain a list of patients with a principal diagnosis of hospital-acquired or healthcare-associated pneumonia discharged in the past month (ICD-9/ICD-10 — Appendix N). Manually review 50 charts (or obtain a list from the microbiology lab) from this list to determine what percentage of patients had sputum cultures performed.
- **Local prevalence:** Acquire a list of respiratory cultures from your microbiology lab obtained from induced and expectorated specimens (non-intubated patients) for the past year. Eliminate duplicate specimens from the same patient. Calculate the percentage due to *Staphylococcus aureus*. If your local prevalence of *Staphylococcus pneumoniae* among floor patients is <10% of all isolates, the negative predictive value of a MRSA nares is  $\geq 96\%$ .



## Section II: In-Depth Analysis of Current Processes and Opportunities for Improvement

### 2. Treatment:

- Obtain a list of patients with a principal diagnosis of pneumonia discharged in the past month (ICD-9/ICD-10 — Appendix N) who received vancomycin empirically. Manually review 30 charts from this list to determine what percentage met IDSA criteria for empiric coverage of MRSA. Use the assessment form provided (Appendix S).
- Obtain a list of patients who received vancomycin in the past month. Manually review 30–50 charts to determine what percentage of these patients met criteria for appropriate vancomycin use by either IDSA guidelines (Appendix R) or simplified CDC criteria (Appendix S).
- Obtain a list from the microbiology lab of patients diagnosed with MSSA bacteremia in the past year. Review all charts for treatment data (or ask the pharmacy for antibiotic administration data for these hospital encounters). Any cases treated with vancomycin for >72 hours in the absence of a severe penicillin allergy present an improvement opportunity.

Performing an institutional assessment can be daunting at first. Remember, you do not have to fix or assess everything at once, and prioritizing an area of care is important and can narrow the scope of the initial assessment. Appendix T can help you through this process.

Your team should reconvene to discuss the assessments as they become available, and review the assessments as you move to improve each of the focus areas. Some assessment assignments may require additional team member support and may need to be broken down into smaller assignments.

## 2. Process Flow Mapping: A Critical QI Tool

Although you may assume you understand the gaps between your current process and best practices, formally mapping the process will almost certainly reveal gaps that would otherwise be overlooked and mapping will also provide your team with a better understanding of the process in general. The members of the team with the most detailed understanding of the best practice will be able to recognize the gaps and highlight them for the team. The assessment questions, presented earlier in this section, can also help team members to recognize the gaps.

Ideally, this process will leave the team with a list of gaps that need to be addressed in order to achieve the team's goals, and this list will be used to create interventions.

For more information on process flow mapping visit the American Society for Quality (ASQ) website. View an example of a process map by going to [www.hospitalmedicine.org/BOOST](http://www.hospitalmedicine.org/BOOST) (within the section "analyze care delivery").

### Task - Complete a Process Map

Choose one of the assessment areas above in which you identified major antibiotic overuse. Identify a key process to map, i.e., ordering urine cultures, or ordering ceftriaxone for pneumonia. Process mapping requires writing down everything that happens in a given process. Often, the major steps of the process are defined first, and then each step is analyzed in detail. In some cases, the major steps in a process can be accurately defined by a single individual (such as the team leader). However, usually, no individual is able to complete a detailed analysis of all the steps. This highlights the importance of the multidisciplinary team in completing this exercise. Creating a process flow map at one of your initial team meetings also serves as a terrific opportunity to engage all team members in the process and gain their buy-in as the group identifies problems and then naturally begins to look for solutions.





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## **Section III:** STEP IN Interventions to Improve Antibiotic Use for Inpatients



### 1. Developing Interventions

Now that you have made a case for improving antibiotic use at your institution, pulled together your multidisciplinary team and understand your current processes regarding antibiotic use, you are ready to think about interventions for improving antibiotic use in inpatients. Your team may consider a variety of interventions for improving antibiotic use, and the STEP IN team offers the following toolkit that addresses many dimensions of antibiotic use that your team has identified for improvement. The following proposed interventions are adopted from the great work that Arjun Srinivasan, MD, and Scott Flanders, MD, have done with hospitalists in a number of clinical environments.<sup>41</sup> Before laying out some potential stewardship interventions, let us take a moment to review the lessons these experts have to teach us about successes and failures of stewardship implementation.

In their pilot studies in 2012, the Centers for Disease Control and Prevention (CDC) and the Institute for Healthcare Improvement (IHI) focused on developing and testing a practical change package that could be used by every healthcare organization in the country. They refined and tested the CDC/IHI Antibiotic Stewardship Framework, which includes a “driver diagram” (Appendix H) summarizing drivers of antibiotic use, as well as key recommended intervention types. They recruited eight pilot hospitals of various sizes and asked them to commit to testing changes related to at least two “primary drivers.”

They uncovered several **keys to success** in stewardship implementation among hospitalists:

- Antibiotic stewardship seen as an important safety initiative
- Positive and trusting relationship of physician champions to physicians
- High-energy work team
- IT support
- Collaborating with infection prevention to improve *C. difficile* rates
- Collaborating with pharmacy network and IT for support in understanding antibiotic cost data and usage

They also identified several **barriers** that were commonly encountered in their pilot sites:

- Difficulties engaging front-line providers
  - Large/multiple groups make centralized communication difficult
  - Nurses are already overwhelmed with work
- Embedding antibiotic review into an already busy process of care
  - High patient loads, no multidisciplinary rounds
- “QI project fatigue” (don’t frame stewardship as a QI project!)
- Leveraging technology support and working with electronic medical records
- Finding personnel time to collect data

The STEP IN team recommends that stewardship interventions embody the following **core principles**:

- **Evidence-based:** A multitude of data exists in antibiotic stewardship interventions, including numerous studies by hospitalist groups. When possible, interventions should focus on “tried and true” strategies that have been shown to be feasible and rewarding for hospitalists.
- **Provider-centered:** The balance of experience by stewardship practitioners shows that engagement of front-line providers is the key to success for any intervention. Interventions should integrate with existing workflows whenever possible, and align with goals of the institution. **Be creative with incentives.** A \$10 coffee card can go a long way toward motivating change.<sup>79</sup>
- **Resource appropriate:** Teams must carefully count the costs before embarking on a large stewardship project. Be sure that your intervention is scaled to the time and resources that are available to your team. You don’t want to start something you can’t finish. Start small, experience success, then scale up later on.
- **Incremental:** Small incremental changes in the diagnosis and treatment of common infections can accumulate into large impact over time. Doing small things consistently is how cultural shifts are made.
- **High-impact potential:** Interventions should focus on the areas of “low-hanging fruit” where “there is nowhere to go but up.” If your hospital has a problem with high rates of *C diff.* infection, then focus first on the antibiotics associated with *C diff.* If your institution has a large nursing home population with constant admissions for “UTI,” then start with targeting asymptomatic bacteriuria.

## 2. Antibiotic Stewardship Intervention Types Best Suited for Hospitalists

### Improving Documentation: Make Current Antibiotic Start/End Dates Visible at the Point of Care (“Take A Stand, Make A Plan”)

Many hospitalist groups suffer from poor documentation and handoffs, especially regarding infection treatment and antibiotic use. When providers rotate frequently, it is often difficult to discern an antibiotic plan from previous notes, and so antibiotics continue indefinitely both inpatient, and then outpatient. After a few days, no one remembers why the antibiotic was started, what it was treating (“Did the patient end up having a UTI or not? Did anyone call the family to ask about symptoms?”), and how long it was supposed to continue. Combine this poor documentation with significant practice variation regarding treatment durations, and the result is a swamp of **antibiotic inertia**. Antibiotics continue for much longer than needed and are never de-escalated with intentionality. Antibiotic allergies are also not correctly documented or evaluated, leading to overuse of broad-spectrum treatment and increased length of stay (see Appendix AE: Penicillin Allergy Assessment).

Interventions to improve documentation of the following four elements can go a long way to improving the antibiotic use in a practice:

- Current antibiotic
- Specifics of antibiotic allergies
- Indication
- Day of treatment and expected duration

Encouraging providers to commit to a duration, and giving them resources to choose wisely, **makes it much easier for later providers to stop the drug** on that date if the patient is clinically improved.

*Using a documentation intervention alone is not likely going to dramatically impact antibiotic use.<sup>80</sup> However, when used in conjunction with provider education/pocket cards with “evidence-based suggested treatment durations” (see intervention #2 below), documentation can be a powerful tool for cutting inappropriate use via raising provider awareness.*

### **Q: What are some ways to make this information visible to the oncoming provider?**

To be effective, the information needs to be visible at the point of care when providers are making ordering decisions during their daily rounds.<sup>41</sup>

- Modify your group’s progress note template to include these elements at the top of the note every day.
- Use real or digital “sticky notes” that are visible to following providers.
- Create a handoff tool or daily sign-out with these elements, updated by the outgoing provider.
- Create an Excel sheet or a daily list maintained by the team pharmacist to track durations for all patients on antibiotics (Appendix U: Pharmacy Daily Rounding List).
- Incorporate stop dates and indications into the drug orders or order sets based on diagnosis.

### **Shortening Treatment Durations: Education, Standardization and Documentation**

From available evidence we know that a majority of inpatients receive excessive durations of antibiotics, which exposes them to increased risk for *C. diff* infection as well as adverse drug events.<sup>8</sup> High-quality data is available that supports shorter antibiotic durations for these common infections (Appendix V).<sup>81</sup>

**Impacting treatment durations in a sustainable way usually requires a multifaceted approach:** 1) Educating providers on appropriate treatment durations, 2) minimizing variations in practice by standardizing processes of care



(order sets, clinical pathways, decision support), and 3) incorporating treatment durations into provider documentation (Intervention #1). Education alone is unlikely to change practice consistently, without a daily reminder or prompt about recommended treatment durations. Often, the intervention team will need to try multiple avenues before settling on a daily reminder that works best in the workflow of your group (see Appendix W: Plan, Do, Study, Act Cycle). Start with **one doctor for one day** and see how it goes. Tweak it, then try again.

### **Q: If you wanted every provider to choose the same treatment duration for the same disease scenario, HOW would you communicate that information?**

Approaches to education about treatment durations can include one or more of the following:

- Talks and lectures in person or online: one-on-one detailing, or group lectures/Grand Rounds, online modules (online lectures to be provided as part of Project STEP IN)
- Case-based discussions
- Posters for rounding rooms
- Educational podcasts
- Weekly email quiz with incentives for completion

Tools for standardizing practice can include one or more of the following:

- Standard treatment algorithms via pocket cards or mobile phone applications. You don't have to reinvent the wheel! Many stewardship programs and websites provide guidelines online for most common infections that will require minimal adaptation for your facility. (See Appendix X for examples.)
- Standard admission order sets with suggested treatment durations and/or linked references within the EMR. (See Appendix Y for examples.)
- Best-practice alerts integrated into the electronic medical record
- Implementation of a procalcitonin-driven algorithm to guide duration in CAP and COPD exacerbations (See Appendix Z for sample procalcitonin algorithms.)

### **The 72-Hour Antibiotic Time-Out Intervention: “Mindful Medicine”**

Self-monitoring is a highly effective behavior change technique and tool in decreasing antibiotic use.<sup>103,104</sup>

Allowing prescribers to self-monitor avoids the “big brother” phenomenon that can trigger dislike toward antibiotic stewardship programs. At 72 hours, the provider should have a great deal more information available to assist with antibiotic guidance than was available to the admitting provider. Antibiotic time-outs have been shown to be associated with significant reductions in antibiotic costs when practiced among Internal Medicine trainees, even if only done twice weekly.<sup>105</sup> You will need to decide WHO will lead the time-out (the provider, the pharmacist or the intervention team) and WHEN it will happen (multidisciplinary rounds, lunch time). During the time-out, providers should focus on the “Golden Rules of Antimicrobial Prescribing” with the acronym MINDME or using the “4 D’s” (see below).<sup>106</sup>

- M** – Microbiology guides therapy whenever possible
- I** – Indications should be evidence-based
- N** – Narrowest spectrum required
- D** – Dosage appropriate to the site and type of infection
- M** – Minimize duration of therapy
- E** – Ensure monotherapy in most cases

The “Time-Out” is a tool to encourage a provider to critically review every patient on antibiotics and ask him/herself four questions (“The 4 D’s”):

- **Diagnosis:** Does the patient have a bacterial diagnosis that requires antibiotics?
- **Drug:** Do I have the right drug and dose? (Covering the bug? Can I change to PO/narrower spectrum?)
- **Duration:** How long do the guidelines recommend treating?
- **Documentation:** Have I documented my plan clearly?

Time-Outs can take multiple forms (Appendix AB):

1. Paper form placed in the chart
2. Online checklist (McGill online Time-Out) (<http://annals.org/article.aspx?articleid=1935743>)
3. A verbal standing checklist as part of multidisciplinary rounds

Again, the intervention team will need to start with one doctor on one day and see how it goes. Learn from any difficulties, tweak it and try it again (Plan, Do, Study, Act Cycle – Appendix W). You will want to have your guidelines handy to help facilitate de-escalation as much as possible.

### 3. Strategies for Provider and Patient Education

Any successful stewardship intervention must involve education. Education for hospitalists can be challenging since most programs do not have times where all the providers gather in a shared physical space. Be creative with your educational forums. Online platforms and modules can be effective. You can do a weekly podcast, or distribute posters or email blasts. Project STEP IN will provide you with the basic content you will need for the treatment of the major inpatient infections, but your facility will need to engage in ongoing updates surrounding local adaptations, policies and interventions that you may implement. Many online and digital resources exist for provider education (see Appendix I).<sup>107</sup> Explore what works at your institution.

Patient education is also crucial to stewardship success. Many providers cite patient expectations as a reason for prescribing antibiotics. Often the patient is given a diagnosis in the emergency room, i.e., pneumonia, that may turn out to be unlikely after 48 hours of clinical data and observation. Perhaps the patient actually has an exacerbation of heart failure in conjunction with a viral upper respiratory infection. Many hospitalists struggle to “unravel” the initial story that the patient may have been told and convince them that they no longer need antibiotics. There is good news for providers:

- Data from the pediatrics and ED literature shows that clinicians often over-estimate parent’s and patient’s demand for antibiotics, when what they really want is reassurance that their child is not seriously ill, an explanation for their symptoms and a clear treatment plan.<sup>108-110</sup>
- Patient satisfaction is generally linked more to communication than to the writing of a prescription.<sup>110,111</sup>
- Patients are hearing and understanding more about the dangers of antibiotic resistance.<sup>112</sup>
- The CDC provides excellent resources for patient education regarding the lack of utility of antibiotics in a variety of common illnesses (<http://www.cdc.gov/getsmart/community/for-patients/common-illnesses/index.html>).



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## Section IV:

# Evaluation: How Will You Know You Are Making a Difference?

Data Collection, Analysis and Presentation



## Introduction

Data collection, analysis and presentation are essential to the success of any antibiotic stewardship program. As Brent James, a nationally recognized leader in quality improvement, says, “People improve what they measure.”

The Project STEP IN team plans to provide a practical approach to data collection and measurement of variables potentially affected by improving antibiotic use.

The outcome measures you collect will depend on the intervention you choose to implement at your facility. See the table below for suggested outcomes for syndrome-specific interventions compiled from the 2016 IDSEA/SHEA Guidelines for Implementing an Antibiotic Stewardship Program, the National Quality Forum Stewardship Playbook and the CDC/IHI pilot studies.<sup>31,81,113</sup>

Process Measures	Outcome Measures
Excess days of therapy	Hospital length of stay/days of hospitalization avoided
Number of antibiotics administered to patients per day (DOT) *	30-day mortality
Proportion of patients compliant with facility-based guideline or treatment algorithm*	Proportion of patients diagnosed with hospital-acquired <i>Clostridium difficile</i> infection*
Proportion of patients with revision of antibiotics based on microbiology data	Proportion of patients with adverse events related to antibiotic treatment
Proportion of patients converted to oral therapy	Proportion of patients with clinical failure (e.g., need to broaden therapy, recurrence of infection)
Standardized antibiotic administration ratio (SAAR)* for hospitals enrolled in the NHSN AU Module	Sequential antibiotic resistance patterns*
Suggested metrics for hospitalist-driven stewardship	
Antibiotic consumption (cost of administration, not purchasing)*	30-Day admission rates for pneumonia and <i>C. diff</i> *
Proportion of patients with a 72-hour antibiotic time out performed*	Patient satisfaction
Proportion of notes and discharge summaries with appropriate antibiotic documentation*	Accurate antibiotic allergy and adverse reaction histories*
Proportion of patients with guideline-concordant culture ordering (e.g., for urine and sputum cultures)	Number of stewardship interventions with providers and/or patients
Provider education interventions and knowledge scores	

\* NQF-suggested measures

### 1. Data Collection and Reporting — Quantitative

Prior to implementing the STEP IN stewardship tool kit, the team must assess the current state of antibiotic use at the hospital. Assessment Item 3 found in Section II.1 suggests more specific metrics based on the type of intervention your team wants to pursue. The following are generic metrics that are useful for all stewardship teams to track.

- **Baseline pre-intervention:** For the preceding year (monthly data as available).  
For your chosen condition, patient location and provider team, you should develop data collection worksheets that you can use to collect baseline information on the following measures:
  - o **Antibiotic consumption in days of therapy (DOT) per 1,000 patient days** — The total sum of all antibiotic days given in a certain floor (easier to obtain), or for a certain diagnosis (more difficult to obtain, but more informative for stewardship). Any dose of a unique antibiotic (IV or PO) administered in a given 24-hour period counts as 1 DOT. For example, if a patient receives ceftriaxone AND azithromycin in 1 day, that would be 2 DOT/1 patient day. If a patient receives a dose of IV ciprofloxacin in the morning, and a dose of PO ciprofloxacin in the afternoon, that would be 1 DOT/1 patient day. The drug data needs to come from pharmacy and the patient stay data from finance at most hospitals.
    - Alternatively, pharmacy costs for antibiotics can be obtained, but this is less accurate than antibiotic administration data as costs fluctuate, and many drug doses are wasted or not administered.
  - o **Length of stay (LOS)** for a given condition, i.e., community-acquired pneumonia or cellulitis. Monthly average among hospitalist patients for the preceding 12 months. The ability to identify “outliers” (5 percent of patients with longest LOS) and separate from your analysis will be helpful. Alternatively, you can measure median instead of mean LOS.
  - o **Incidence/prevalence of hospital-onset *C. difficile* infections (CDI)**. This data is already being collected in your facility by the Infection Control or quality department. Work with them to determine your facility’s Standardized Incidence Ratio (SIR) and on which floors the most cases of CDI are occurring.
  - o **Other metrics depending on your intervention** (Section II.1, Assessment Item 3)
- **Post-implementation:** After piloting and fully implementing the tool kit, data should be collected and reported on a monthly basis using data sheets.
  - o For example, project targeting treatment duration for CAP could display percentage of patients with a 72-hour Time-Out, summary of Time-Out interventions, inpatient and total treatment durations, percentage utilization of fluoroquinolones, LOS and 30-day readmission rates.

### 2. Data Collection and Reporting — Qualitative

Describe your activities from a qualitative perspective. The following strategies/activities may assist in sharing key perspectives regarding outcomes from program implementation:

- Document team member participation and meetings with your senior hospital administration.
- Disseminate reports about your project to local media.
- Describe barriers you encountered and how they were handled.

As you implement the stewardship intervention, your team will need to assess if your efforts are leading to the desired changes in practice.

- When you uncover a change in prescribing practices, it is important to investigate its root causes. Perhaps drug resistance patterns or national guidelines have changed or the floor has experienced high provider turnover. Such qualitative assessment will allow you to better understand why implementation is working or not.
- When positive gains are observed, develop channels to report your findings “up the chain” to hospital administration in order to keep funding sources open and potentially expand interventions to other services or disease states.
- Also report any positive gains “down the chain” to front-line providers to encourage and motivate prescribers to keep doing good work.



### **3. Trending Data Over Time: Run Charts and Statistical Process Controls**

A run chart displays data in a graph format as results occur over time. The y axis (vertical) represents the result you are measuring, and the x axis (horizontal) represents time. In this project, for example, a run chart could display length-of-stay averages or 72-hour Time-Out rates on a monthly basis (see Appendix AC).

Run charts allow the opportunity to readily identify variation in data that suggest changes in a process over time. A run chart may contain a straight line showing the average in order to more readily visualize deviations. Run charts can be modified into control charts using statistical process control by placing the control limits of the process.

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## Section V: Continuing to Improve



### 1. Monitoring and Learning from Variation in the Process

After the launch of your interventions: Just the beginning!

At this point you should have launched your interventions to improve antibiotic use at your hospital. What you do after this point is equally critical to the long-term success and sustainability of the initiative. The team needs to devise a way to track barriers and issues encountered during the implementation process.

Practice that varies from your expectations of the intervention process may occur for any of several reasons:

- A special patient population at your hospital falls outside of the reach of your intervention (i.e., a large percentage of immunocompromised patients)
- Old habits/lack of knowledge/unwillingness to change
- The new interventions are too hard to incorporate into the provider workflow
- Social determinants of antibiotic use at your hospital (prescriber etiquette, inertia)
- Providers may not agree with a standardized approach to care

As you track variation, it will become important to determine which variation is appropriate and which is not. There will be patients who do not fit into your intervention process. If you are finding that this is occurring more frequently than expected, it may be worth building in methods for end users to clearly document why these patients are “different.”

This documentation will allow you to more easily identify appropriate variation as well as to assure that the reasons given for being “different” are appropriate. If you find that some of the tools are difficult to use or that some processes are cumbersome, your team may need to reexamine the intervention and determine what components may need to change.

Some behaviors will require incentives to bring care into compliance with your standardized approach. A combination of positive and negative incentives may be required to improve compliance. Improving appropriate use of the intervention also may require increased educational efforts by your team to improve understanding of the rationale behind the standardized recommendations.

However, if you do not look for variation, you will not find it. Similarly, if you do not determine why there is variation, you will not be able to adequately address issues that will improve compliance. With ongoing monitoring of the intervention, you will be able to better respond to valid issues by adjusting tools and processes and reducing inappropriate variability by a combination of correction methods.

### **TASK**

Devise methods to track deviation from your intervention bundle. Revise your intervention on the basis of feedback from users and patient needs.

Task Assignment: \_\_\_\_\_

Time Line for Completing: \_\_\_\_\_

Repeat in a continuous manner.

## **2. Holding the Gains and Spreading Your Improvement**

### **Holding the Gains**

Once you have changed prescribing patterns in your target area, it may be tempting to move on to other issues and to stop monitoring the process. But if you don't want all your hard work to go to waste, you need to resist this temptation. Do not assume the antibiotic prescribing culture is "fixed" simply because you implemented your intervention. To hold and spread the gains you've accomplished, you must keep monitoring the process so your improvements will not erode. Although you may be able to reduce the intensity of the monitoring and modification process, some ongoing assessment of how the process is functioning is absolutely necessary. In addition, new findings from research publications, new therapies and new patient situations arise frequently. The team should remain responsible for monitoring these issues, updating your tools and processes, and revising the intensity of scrutiny based on the stability of your metrics.

### **TASK A**

Schedule regular assessments to monitor and trend your metrics. Schedule interval reviews of the literature. Schedule sessions to update the protocol/order set.

Task Assignment: \_\_\_\_\_

Time Line for Completing: \_\_\_\_\_

### **Spreading the Improvement**

Creating breakthrough levels of improvement is hard work, but it also can be exciting and rewarding. Ideally, others will learn from your experience and implement your interventions in their own environment at an accelerated pace while still allowing for customization to account for their own unique setting. The improvement in antibiotic use in your target population can serve as a model for other areas in your organization. The IHI website has a detailed discussion of a framework to enhance spread of innovations throughout an organization. (See Appendix AD: Statistical Process Control Chart: Institute for Healthcare Improvement.)

[www.ihl.org](http://www.ihl.org)

### **TASK B**

Identify the priority areas to “spread” the improvements you have achieved. Review the framework for spread on the IHI website. Don’t overlook this significant opportunity.

Task Assignment: \_\_\_\_\_

Time Line for Completing: \_\_\_\_\_



# Fight The RESISTANCE



## Appendices



## Appendix A. List of Websites Used in the Implementation Guide

42 CFR Part 412 Medicare Program; Inpatient Rehabilitation Facility Prospective Payment System for Federal Fiscal Year 2016. Proposed rule

(<https://www.gpo.gov/fdsys/pkg/FR-2015-04-27/pdf/2015-09617.pdf>)

CMS.gov Home page for Proposed Changes to the Inpatient PPS for Acute Care & the Long-Term Care PPS & FY 2015 Rates

(<https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/HospitalAcqCond/HAC-Regulations-and-Notices.html>)

IDSA Home page for Hospital Acquired Conditions Payment Policies

([http://www.idsociety.org/Hospital\\_Acquired\\_Conditions/](http://www.idsociety.org/Hospital_Acquired_Conditions/))

CDC Patient Education Page for Antibiotic Stewardship. “Get Smart: Common Illnesses”

(<http://www.cdc.gov/getsmart/community/for-patients/common-illnesses/index.html>)

## Appendix B: Sample Analyses for Projected Cost Savings Based on Intervention Type

These models are theoretical projections based on numerous assumptions and are intended to serve as food for thought rather than precise templates to follow.

Administrators should understand that the biggest cost savings will be apparent in year 1, but that if the program does not continue, costs will rebound back to pre-intervention levels.<sup>1</sup>

Many sophisticated and comprehensive methods for cost effectiveness of stewardship interventions are available in the literature. Below are examples of more straightforward cost analyses that are more easily reproduced:

- Dik, et al., 2015.<sup>2</sup> “Cost-minimization model of a multidisciplinary antibiotic stewardship team based on a successful implementation on a urology ward of an academic hospital.” — A nice study showing a comprehensive accounting of personnel time and drug costs accompanying a 48-hour time-out process.
- Day, et al., 2015.<sup>3</sup> “An Infectious Diseases Physician-Led Antimicrobial Stewardship Program at a Small Community Hospital Associated With Improved Susceptibility Patterns and Cost-Savings After the First Year.” — A simple and straightforward calculation of drug cost savings using a once-weekly ID physician stewardship consultant in a small rural hospital.
- Chowdhury, et al., 2012.<sup>4</sup> “Preventing the inappropriate treatment of asymptomatic bacteriuria at a community teaching hospital.” — A protocol implementation strategy with basic cost savings data.

See below for tips on creating a quick and usable model of cost savings to assist in your bid for institutional support of a stewardship intervention.

### Sample Analysis 1: Decreasing piperacillin/tazobactam usage in cellulitis

Source of cost savings: A large percentage of cases of uncomplicated cellulitis are treated with expensive agents with gram-negative coverage that is not necessary, i.e., piperacillin/tazobactam or meropenem.<sup>5</sup>

#### Assumptions

1. Exclude all complicated cases using ICD-9 codes (See Appendix N).
2. Baseline case: 60% of inpatients hospitalized with cellulitis are receiving gram-negative coverage with piperacillin/tazobactam, and 5% with ampicillin-sulbactam for an average of 5 days in house.
3. Appropriate average inpatient duration should be 3 days (with additional 3–5 days PO on discharge).
4. Around 30-50% of hospitalized patients meet criteria for gram-negative coverage (“complicated cases”<sup>6</sup>), but this can be provided with ampicillin/sulbactam when *Pseudomonas* is not suspected (i.e., almost always except for burns).
5. The number treated with piperacillin/tazobactam or meropenem should be relatively small (i.e., <10%), unless your hospitalist group cares for a burn unit or sees a lot of trauma/necrotizing post-operative wounds with resistant gram-negatives.
6. Cost of piperacillin/tazobactam = \$36/day; cost of ampicillin/sulbactam = \$11/day

	Cellulitis cases/year	Piperacillin / tazobactam			Ampicillin/sulbactam			Avg duration (days)	Cost/case (GNR coverage)	Annual cost	Annual cost savings
		(n)	%	Total Cost	(n)	(%)	Total Cost				
Baseline period	600	360	60%	\$64,800	30	5%	\$1,650	5	\$132.90	\$79,740	Reference
Intervention: sub amp/sulbactam	600	30	5%	\$5,400	360	60%	\$19,800	5	\$50.40	\$30,240	\$49,500
Intervention: shorten duration	600	360	60%	\$38,880	30	5%	\$990	3	\$79.74	\$47,844	\$31,896
Intervention: drop % with GNR coverage	600	120	20%	\$21,600	120	20%	\$6,600	5	\$56.40	\$33,840	\$45,900
Intervention: All 3	600	120	20%	\$12,960	120	20%	\$3,960	3	\$33.84	\$20,304	\$59,436

### Sample Analysis 2: Streamlining therapy for CAP with risk for drug-resistant pathogens (formerly known as “HCAP”)

Source of cost savings: A large number of patients with a diagnosis of CAP with risk factors, i.e. healthcare contact, are often started on empiric broad antibiotics (i.e., vancomycin and piperacillin/tazobactam) that are never de-escalated to narrower agents (i.e., ceftriaxone, moxifloxacin), despite mild/moderate illness and clinical improvement. Sputum cultures are relatively expensive, but the benefit of *C. diff* prevention can outweigh the costs.

#### Assumptions:

1. Baseline case: 60% of patients admitted with HCAP are treated with vancomycin (\$11/day) and piperacillin/tazobactam (\$36/day) and continued for 5 days without de-escalation. 20% get sputum cultures done (\$136), and 10% have a MRSA nares done. 10% of patients receive ceftriaxone alone (\$2/day).
2. Sputum cultures cost \$136 each and allow for discontinuation of vancomycin and piperacillin/tazobactam in a vast majority of cases, changing to an oral therapy.
3. A negative MRSA nares has a negative predictive value >95% for MRSA in respiratory infections and costs \$50 for a PCR-based assay.<sup>7,8</sup> Vancomycin can be stopped after a negative MRSA nares result on day 2.
4. Sputum cultures in patients with HCAP grow drug-resistant pathogens 12%–15% of the time,<sup>9-12</sup> and a majority of these can be predicted with risk stratification algorithms.<sup>12,13</sup>

- 5. Using risk stratification tools, empiric broad-spectrum therapy can be safely avoided in 50% of HCAP patients.<sup>12</sup>
- 6. Risk of *C. diff* in 60 days for patients treated with  $\geq 7$  antibiotic days of therapy = 2.73%, compared to a 1.32% risk for patients treated with  $\leq 7$  days of therapy.<sup>14</sup>
- 7. Each community onset case of *C. diff* costs \$1,400 to treat (Vanco 125 mg PO q6 x 14 days), which represents 75% of cases. Hospital onset cases (25%) increase costs by \$7,800/case.<sup>15</sup>

	HCAP cases/year	Sputum cultures	Cost	MRSA nares	Cost	Vancomycin				Piperacillin-tazobactam				Ceftriaxone			
						(n)	%	Days	Total Cost	(n)	(%)	Days	Total Cost	(n)	%	Days	Total Cost
Baseline period	400	20%	\$12,000	10%	\$2,000	240	60%	5	\$12,000	240	60%	5	\$43,200	80	20%	5	\$800
Intervention: Vanc de-escalation-MRSA nares	400	20%	\$12,000	90%	\$18,000	240	60%	2	\$4,800	240	60%	5	\$43,200	80	20%	5	\$800
Intervention: Risk stratify empiric tx	400	50%	\$30,000	10%	\$2,000	120	30%	5	\$6,000	120	30%	5	\$21,600	280	70%	5	\$2,800
Intervention: Culture driven de-escalation	400	80%	\$48,000	0%	\$0.00	240	60%	3	\$7,200	240	60%	3	\$25,920	120	30%	5	\$1,200

	Cumulative abx days/patient (Vanc + pip/tazo group)	Patients	Cumulative abx days/patient (CTX group)	Patients	<i>C. diff</i> cases within 60d	<i>C. diff</i> cost	Total annual cost	Relevant cost/case	Annual cost savings
Baseline period	10	240	5	80	7.608	\$47,169.60	\$117,170	\$292.92	Reference
Intervention: Vanc de-escalation	7	240	5	80	6.72	\$41,664.00	\$120,464	\$301.16	-\$3,294
Intervention: Risk stratify empiric tx	10	120	5	280	6.972	\$43,226.40	\$105,626	\$264.07	\$11,543
Intervention: Culture driven	6	240	5	120	4.752	\$29,462.40	\$111,782	\$279.46	\$5,387

### Sample Analysis 3: Reducing urine cultures and antibiotic treatment for asymptomatic bacteriuria

Source of cost savings: In patients without guideline-concordant symptoms of UTI, both urine cultures and antibiotics can be avoided, which has the potential for huge cost savings given the number of urine cultures sent in most hospitals.

#### Assumptions:

1. Baseline case: On the inpatient medical wards, 250 urine cultures are ordered each month (JHBMC data).
2. Urine cultures cost \$140 (Google search).
3. Of ordered cultures, 50% have a guideline-based indication for culture ordering.<sup>16,17</sup>
4. Of ordered cultures, 30% (n=80) are positive for pathogens (JHBMC data).
5. Of the positive cultures, 60% represent asymptomatic bacteriuria (ABU) (extrapolated<sup>17</sup>).
6. The most common inpatient drugs for empiric treatment of UTI in hospitalized patients are ceftriaxone (75%) and ciprofloxacin (25%) — this is conservative; cefepime and other broad-spectrum drugs are often used and would show more cost savings.
7. Of the asymptomatic bacteriuria, 60% of these receive antibiotics for a mean of 9 days (extrapolated<sup>17</sup>).
8. An educational intervention among hospitalists can reduce treatment of ABU by 20–30%.<sup>18,19</sup> Extrapolate same impact of urine culture ordering, 30% reduction post-intervention.

	Urine cultures/ month	Total cost	Appropriate cultures	+ucx	ABU	ABU treated	Ceftriaxone			Ciprofloxacin			Duration (days)	Annual cost	Annual cost savings
							(n)	%	Total Cost	(n)	(%)	Total Cost			
Baseline period	250	\$35,000	125	83	50	30	22	75%	\$401	7	25%	\$735	9	\$433,632	Reference
Intervention: Reduce inappropriate ucx orders	165	\$23,100	125	54	33	20	15	75%	\$265	5	25%	\$485	9	\$286,197	\$147,000
Intervention: Reduce treatment of ABU	250	\$35,000	125	83	50	20	15	75%	\$208	5	25%	\$381	7	\$427,069	\$6,128
Intervention: Both	165	\$23,100	125	54	33	13	10	75%	\$137	3	25%	\$252	7	\$281,865	\$151,332

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6. Jenkins TC, Sabel AL, Sarcone EE, Price CS, Mehler PS, Burman WJ. Skin and soft-tissue infections requiring hospitalization at an academic medical center: opportunities for antimicrobial stewardship. *Clin Infect Dis*. 2010;51(8):895-903.
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19. Hartley SE, Kuhn L, Valley S, et al. Evaluating a Hospitalist-Based Intervention to Decrease Unnecessary Antimicrobial Use in Patients With Asymptomatic Bacteriuria. *Infect Control Hosp Epidemiol*. 2016;6:1-8.

## Appendix C: Sample Letter to Hospital Administration for Support of Hospitalist Stewardship Intervention

Dear \_\_\_\_\_,

As hospitalists, we are committed to the highest quality of care for our patients, which includes the optimal use of antibiotics for patients with infections through antimicrobial stewardship. Excess antibiotic use has numerous adverse impacts both on patients, and on the hospital as a whole. Studies have shown that up to 50% of all antibiotics prescribed in the inpatient setting are unnecessary and inappropriate.<sup>1</sup> Inappropriate antibiotic use is associated with an increase in drug-resistant infections, leading to increases in length of stay, mortality, and excess hospital costs of nearly \$30,000 in certain cases.<sup>2</sup> Antibiotics are one of the top medication classes resulting in emergency department visits for adverse drug events each year<sup>3</sup> which can also increase healthcare costs.

Antimicrobial stewardship programs aim to optimize antibiotic use for patients with infections and reduce unnecessary antibiotic use. These programs have been associated with large reductions in pharmacy costs<sup>4-6</sup> and *C. difficile* cases<sup>7</sup> while improving patient outcomes,<sup>8</sup> and can become self-sustaining over time, though that is a secondary consideration to the patient outcomes measures.<sup>9</sup>

In addition to the incentives of improving patient care and saving costs, The Joint Commission has issued a requirement to include presence of a hospital antimicrobial stewardship program in the standards for hospital accreditation.<sup>10</sup>

Given the proven benefits of antimicrobial stewardship activities, our hospitalist group is seeking the support of the hospital to help improve the state of antimicrobial prescribing at our hospital. Attached is a summary of the current state of antibiotic use at our hospital, opportunities for improvement, and a brief proposal of our intervention.

In the interest of optimizing the care of our patients, I/we would like to request:

(choose most appropriate)

A meeting at your earliest convenience to discuss this topic and how improving antibiotic use could align with the strategic goals for our organization

A meeting of stakeholders including \_\_\_\_\_ to discuss next steps in improvement of antibiotic use

I/we look forward to further discussions with you.

Sincerely,

(Project Team Members)



## Additional Resources:

GNHYHA Antimicrobial Stewardship Toolkit – Appendix N “Administrator-Oriented PowerPoint Presentation” [<https://www.gnyha.org/whatwedo/quality-patient-safety/infection-control-prevention/antimicrobial-stewardship>]

## References

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2. Cosgrove SE, Kaye KS, Eliopoulous GM, Carmeli Y. Health and economic outcomes of the emergence of third-generation cephalosporin resistance in *Enterobacter* species. *Arch Intern Med.* 2002;162(2):185-190.
3. Jones SC, Budnitz DS, Sorbello A, Mehta H. US-based emergency department visits for fluoroquinolone-associated hypersensitivity reactions. *Pharmacoepidemiol Drug Saf.* 2013;22(10):1099-1106.
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5. Hayman JN, Sbravati EC. Controlling cephalosporin and aminoglycoside costs through pharmacy and therapeutics committee restrictions. *Am J Hosp Pharm.* 1985;42(6):1343-1347.
6. Agwu AL, Lee CK, Jain SK, et al. A World Wide Web-based antimicrobial stewardship program improves efficiency, communication, and user satisfaction and reduces cost in a tertiary care pediatric medical center. *Clin Infect Dis.* 2008;47(6):747-753.
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10. The Joint Commission. Standard MM.09.01.01. “Proposed Standard for...Obs.” URI: [https://jointcommission.az1.qualtrics.com/CP/File.php?F=F\\_5tDHGzIVDMHenDn](https://jointcommission.az1.qualtrics.com/CP/File.php?F=F_5tDHGzIVDMHenDn). Accessed 1/17/16

## Appendix D: Tool for Identifying Key Stakeholders, Committees and Groups



### TASK A

Identify key stakeholders, committees and special groups that need to be aware of your efforts to improve the discharge care transition. You also need to understand where your team fits into the organization's quality improvement structure. This understanding is critical, especially if the group identifies barriers that require broader organizational support to overcome. In addition, clarifying this relationship will assist other QI teams and will help to standardize the approach to clinical care improvement.

**Stakeholders:**

**Committees:**

**Special Groups (including consumer groups):**

Assignment for Task A \_\_\_\_\_ (Team Leader)

Time Line for beginning and completing: \_\_\_\_\_



### TASK B

Clarify the reporting structure and approval process for your interventions, and resource approval (include names, titles, and if helpful, an organizational chart that reflects the process).

**Reporting Structure:**

**Approval Process:**

Assignment for Task B \_\_\_\_\_ (Team Leader)

Time Line for beginning and completing: \_\_\_\_\_

## Appendix E: Content Expert Annotated Bibliography

### The Urgency of Antimicrobial Stewardship in Inpatients

1. “ANTIBIOTIC RESISTANCE THREATS in the United States, 2013” [<http://www.cdc.gov/drugresistance/threat-report-2013/pdf/ar-threats-2013-508.pdf#page=13>]
  - a. This document is the definitive CDC-issued summary of national-level data on rising rates of antibiotic resistant infections and *Clostridium difficile*. The data was derived a 2009-2011 analysis of government datasets including the National Antimicrobial Resistance Monitoring System (NARMS), the Emerging Infection Program (EIP)/Active Bacterial Core (ABC) Surveillance program, and the National Healthcare Safety Network Reports on Antimicrobial Resistance and Hospital Acquired Infections. Written in an accessible way for multiple audiences, great graphics for presentations, and a technical appendix with references.
2. National Action Plan for Combating Antibiotic-Resistant Bacteria, March 2015. [[https://www.whitehouse.gov/sites/default/files/docs/national\\_action\\_plan\\_for\\_combating\\_antibiotic-resistant\\_bacteria.pdf](https://www.whitehouse.gov/sites/default/files/docs/national_action_plan_for_combating_antibiotic-resistant_bacteria.pdf)]
  - a. This White House Report followed the 2014 Report to the President on Combating Antibiotic Resistance issued by the President’s Council of Advisors on Science and Technology (PCAST), which detailed the rise of resistance in the USA. The President responded with Executive Order No. 13676 (Combating Antibiotic-Resistant Bacteria) which called the Department of Health and Human Services (DHHS) to promote antibiotic stewardship programs (ASPs) formation and implementation nationwide. The National Action Plan established antimicrobial stewardship goals, including reducing *C. diff* by 50%, hospital acquisition of MDR *Pseudomonas* by 35%, reduce MRSA bloodstream infections by 50%, and inappropriate antibiotic use in inpatients by 50%. The Council recommended that within 3 years (by 2017), all hospitals have a CDC-compliant ASP as a condition of Medicare participation. They also recommended that the CDC establish benchmarks for antibiotic utilization rates, that states collect data on healthcare facilities with “high antibiotic-prescribing rates” and strive to apply best practices to these facilities.
3. Proposed CMS Measures on Antibiotic Stewardship: Medicare Program; Hospital Inpatient Prospective Payment Systems for Acute Care Hospitals and the Long-Term Care Hospital Prospective Payment System and Proposed Policy Changes and Fiscal Year 2017 Rates [<https://www.federalregister.gov/articles/2016/04/27/2016-09120/medicare-program-hospital-inpatient-prospective-payment-systems-for-acute-care-hospitals-and-the>]
  - a. Includes a proposal to make hospital antibiotic prescribing data available to CMS for Quality Reporting, using data submitted via the National Healthcare Safety Network (NHSN) Antimicrobial Use Module
  - b. Includes a proposal to compare hospital antibiotic use to national benchmarks

4. NQF-Endorsed Measure #2720: NHSN Antimicrobial Utilization [<http://www.qualityforum.org/QPS/2720>. <http://www.cdc.gov/nhsn/PDFs/pscManual/11pscAURcurrent.pdf>]
  - a. This measure permits hospital benchmarking of antibiotic use through the Standardized Antimicrobial Administration Ratio (SAAR), which is a risk-adjusted measure comparing observed antibiotic use to expected use given patient location and drug. This measure is derived from data inputted through the NSHN AUR Module. Calculation starts with antibiotic days of antibiotic therapy (DOT) (any antibiotic dose given in a 24 hour period to a given patient) and 1000 patient days (any patient present on that unit during the same day). This ratio will standardized based on aggregate national averages for antibiotic use on “comparable units” in all hospitals.

## The Benefits of Antimicrobial Stewardship Programs

1. Schuts et al. “Current evidence on hospital antimicrobial stewardship objectives: a systematic review and meta-analysis.” Published online March 2, 2016 [[http://dx.doi.org/10.1016/S1473-3099\(16\)00065-7](http://dx.doi.org/10.1016/S1473-3099(16)00065-7)]
  - a. This article is the largest and most recent systematic review and meta-analysis of the impact of stewardship on patient outcomes. It asks the question: does achieving specific antimicrobial stewardship objectives improve clinical outcomes, adverse events, costs, and bacterial resistance rates? 14 stewardship objectives were evaluated, and the following were found to significantly improve patient outcomes:
    - Empiric therapy according to guidelines → Relative reduction in mortality 35% ( $p < 0.0001$ )
    - De-escalation of therapy → Relative reduction in mortality 66% ( $p < 0.0001$ ) – Data is low quality as most studies are retrospective and the one RCT did not show a difference in antibiotic use between groups. Data in the literature for procalcitonin-driven de-escalation is much better than protocol-driven de-escalation.
    - IV to PO conversion
    - Therapeutic drug monitoring
    - Antimicrobial restriction
    - Bedside ID consultation for *Staphylococcus aureus* bacteremia

## Hospitalist Successes as Antibiotic Stewards

Other projects are reviewed in Rohde et al. “Role of the Hospitalist in Antimicrobial Stewardship: A Review of Work Completed and Description of a Multisite Collaborative.” *Clinical Therapeutics*. 2013;35(6):751-757.

1. Kisuule et al., “Improving antibiotic utilization among hospitalists: A pilot academic detailing project with a public health approach.” *J. Hosp. Med.* 2008;3(1):64–70.
  - a. A nice project from Johns Hopkins Bayview demonstrating the effectiveness of provider education/ individual detailing sessions in improving appropriateness of antibiotic use among hospitalists. This project was conducted as a team effort between an ID consultant and the hospitalists. The ID consultant helped to develop appropriateness criteria for antibiotic use and the hospitalist group undertook to feedback that information to prescribers. Appropriate prescriptions went from 43% to 74% after the intervention. Good discussion of a conceptual model of prescriber behavior.

2. Kiyatkin et al. 2011. "Improving utilization of antimicrobial drugs among physician assistants in the ED." *JAAPA*. 2011;24(10):44.
  - a. At Johns Hopkins Bayview, the hospitalist leaders conducted an educational intervention among ED physician assistants to improve compliance with institutional guidelines ("appropriate prescribing") in 4 common infections: SSTI, pneumonia, UTI's, abdominal infections. The intervention involved a 1-hour detailing session with each PA. The total number of inappropriate antibiotic orders dropped from 35% to 19% in the post-intervention period ( $p < 0.001$ ).
3. Alvarez et al. 2012. "Antimicrobial Stewardship on the Hospitalist Service: Skin and Soft Tissue Infections." *SHM Abstracts*- <http://www.shmabstracts.com/abstract/antimicrobial-stewardship-on-the-hospitalist-service-skin-and-soft-tissue-infections/>.
  - a. In this report, the hospitalist group, working with ID and pharmacy, developed an intervention for uncomplicated cellulitis to decrease usage of ticarcillin/clavulanate. Their intervention was multifaceted including provider education, a pocket card, and provider feedback via report card. In 41 cases, there was a 60% decrease in broad-spectrum use ( $p = 0.0016$ ).
4. Mack et al. "Engaging hospitalists in antimicrobial stewardship: Lessons from a multihospital collaborative." *J Hosp Med*. 2016 Apr 30.
  - a. This paper is the result of a multi-year 5-hospital CDC/IHI collaborative, spearheaded by Arjun Srinivasan, MD (CAPT, USPHS) and operationalized with the help of Scott Flanders, MD (hospitalist at University of Michigan). The paper contains essential information about barriers and facilitators of hospitalist stewardship in their experience. This paper is, at this point, the largest study demonstrating the effectiveness of hospitalist-driven stewardship. It contains process measures, but not outcome measures, which are still lacking in the literature. A must-read. The supplemental material contains details about the pocket card they used.
5. Hartley et al. "Evaluating a Hospitalist-Based Intervention to Decrease Unnecessary Antimicrobial Use in Patients With Asymptomatic Bacteriuria." *Infect Control Hosp Epidemiol*. 2016 Jun 6:1-8. [Epub ahead of print]
  - a. A secondary report from the multisite IHI/CDC collaborative on hospitalist stewardship, this study demonstrated that a hospitalist education intervention could have a 20% decrease in the treatment of asymptomatic bacteriuria and a reduction in antibiotic use. Pharmacy involvement was critical to success. A pocket card with UTI diagnosis criteria and treatment recommendations are displayed in the article.

## Antibiotic Stewardship Examples in Hospitalized Patients with Cellulitis

1. Jeng et al. "The role of beta-hemolytic streptococci in causing diffuse, non-culturable cellulitis: a prospective investigation." *Medicine*. 2010;89(4):217-226.
  - a. A prospective study of "diffuse non-culturable cellulitis" between 2004-2007 in UCLA. The authors evaluated blood cultures, acute and convalescent ASO titers/DNAse B, and response to beta-lactams. They excluded culturable sources - abscess, wound, or ulcer as well as periorbital, perineal, and groin, bite wounds, neutropenic patients, necrotizing fasciitis, myositis, osteomyelitis, prior pharyngitis/SSTI in past year (due to serology confounding). Results: n=179. 73% had beta-hemolytic strep (BHS). Of those that had e/o BHS, 97% responded to beta-lactams. Of those that did not have confirmed BHS, 91% responded to beta-lactams! (Overall response rate = 95.8%).
2. Jenkins et al. "Decreased antibiotic utilization after implementation of a guideline for inpatient cellulitis and cutaneous abscess." *Arch Intern Med*. 2011;171(12):1072-1079.
  - a. A prospective study of the impact of a clinical pathway + order set on reducing gram-negative coverage for uncomplicated cellulitis. They recommended vancomycin for both purulent and non-purulent cellulitis and a treatment duration of 7 days. They excluded all complicated cases including chronic wounds, venous stasis, PAD, ICU admission or severe sepsis, bacteremia, deep tissue infection/NF, surgical wound, indwelling medical device, hospitalization or long-term care within 90 days, need for fascial biopsy, recurrent cellulitis, human or animal bite, perirectal abscess or cellulitis, periorbital or orbital cellulitis, odontogenic infection. Of note, this excluded over HALF of all the skin and soft tissue infections that were admitted (436/780=56%). They saw a significant drop in gram-negative coverage (from 66% to 36% of cases, p<0.001) in the patients they evaluated, without an increase in clinical failures.
3. Jenkins et al. "Skin and soft-tissue infections requiring hospitalization at an academic medical center: opportunities for antimicrobial stewardship."
  - a. A descriptive study of a cohort of consecutive adult patients hospitalized for SSTI in 2007 at Denver Health. 322 patients included. These were divided into mutually excluded categories: cellulitis (66/322 = 20%, cutaneous abscess (103/322 = 32%), and "SSTI with complicating factors" (153/322 = 48%)(deep tissue infection, bacteremia, ICU admission, diabetic ulcer or chronic ulcer, PAD, recurrent cellulitis, bites, severe cellulitis requiring surgical debridement, necrotizing fasciitis, periorbital or perirectal, hospitalization/LTAC/ surgery in past 90 days. Cultures were reviewed if they were obtained from deep tissue, abscess cavity, blood cultures. Cultures not reported for cellulitis NOS. Abscess cultures were mainly staph/strep, but polymicrobial/ mixed, SSTI with complicating factors was still mainly staph and strep.

### Antibiotic Stewardship Examples in Hospitalized Patients with Community-Acquired Pneumonia

1. el Moussaoui R, et al. “Effectiveness of discontinuing antibiotic treatment after three days versus eight days in mild to moderate-severe community acquired pneumonia: randomised, double blind study.” *BMJ*. 2006; 332(7554):1355.
  - a. A RCT in the Netherlands to compare 3 days of antibiotics versus 8 days for CAP – mild to moderate/severe. Exclusions: HIV CD4<200, HCAP, neutropenia, aspiration, possible empyema, atypical/*Staph aureus*/*Klebsiella*. All patients received IV amoxicillin x 3 days. At 3 days patients were randomized into 2 groups if they had improvement, afebrile, and could take PO. Group 1 (n=64) --> amoxicillin 750 mg PO TID x 5 days (8d total); Group 2 (n=56) --> placebo. Results: Clinical cure at 10 days was 93% in both groups. Clinical cure per protocol at 28 days was higher in the 3-day group (90% vs 88%) with less adverse events (11% vs 21%).
2. Avdic 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.
  - a. Conducted at Johns Hopkins Hospital, this prospective study primarily tested the impact of provider education on treatment duration for CAP. They saw a significant drop in treatment duration from 10 days to 7 days, more de-escalation, and less duplicate therapy. The intervention included a knowledge survey, a lecture, and phone calls from the stewardship team to the primary providers with feedback suggesting changes. This intervention was really an ID pharmacy-driven feedback process, which would be labor intensive for a physician in a large group, but doable with pharmacy help.

### Antibiotic Stewardship Examples in Hospitalized Patients with Urinary Tract Infections

1. Trautner et al. “Effectiveness of an Antimicrobial Stewardship Approach for Urinary Catheter-Associated Asymptomatic Bacteriuria.” *JAMA Intern Med*. 2015;175(7):1120.
  - a. The largest and most comprehensive study published on stewardship in CAUTI. Trautner and her team at 2 different VA sites (inpatient and long term care) engaged in 3-year “multifaceted guidelines implementation intervention” which included provider education about appropriate urine culture ordering and treatment, with an emphasis on not culturing or treating asymptomatic patients. The team distributed a diagnostic algorithm for CAUTI and used case-based audit and feedback (with an interactive PowerPoint for each case) to train clinicians to use it. Urine culture ordering and overtreatment dropped dramatically in the post-intervention period.
2. Hartley et al. “Evaluating a Hospitalist-Based Intervention to Decrease Unnecessary Antimicrobial Use in Patients with Asymptomatic Bacteriuria.” *Infect Control Hosp Epidemiol*. 2016 Jun 6:1-8. [Epub ahead of print]
  - a. A secondary report from the multisite IHI/CDC collaborative on hospitalist stewardship, this study demonstrated that a hospitalist education intervention could have a 20% decrease in the treatment of asymptomatic bacteriuria and a reduction in antibiotic use. Pharmacy involvement was critical to success. A pocket card with UTI diagnosis criteria and treatment recommendations are displayed in the article.

### Antibiotic Stewardship Examples in Hospitalized Patients with Suspected MRSA

1. Kumana et al. “Curtailing unnecessary vancomycin usage in a hospital with high rates of methicillin resistant *Staphylococcus aureus* infections.” *Br J. Clin Pharmacol.* 2001;52(4):427-432.
  - a. While this is an older study, it is one of the few that actually reports patient outcome data after instituting a vancomycin use policy that was concordant with HICPAC guidelines. The stewardship team reviewed all cases of vancomycin/ teicoplanin use and left a memo in the chart alerting providers of “errant” prescriptions and encouraging discontinuation. Vancomycin use decreased by almost half (76 to 45 defined daily doses/1,000 admissions). Importantly, mortality for staphylococcal bacteremia remained unchanged, despite the fact that 33% of all their staph isolates were MRSA.
2. Boyce et al. 2013. “A trial of discontinuation of empiric vancomycin therapy in patients with suspected methicillin-resistant *Staphylococcus aureus* health care-associated pneumonia.”
  - a. This study is extremely useful in HCAP because the authors demonstrated that is safe to discontinue empiric vancomycin based on negative throat and nares cultures for MRSA when respiratory cultures were not available. They note that the severity of illness was low in the de-escalated patients (97% had a CPIS  $\leq 6$  on the day of de-escalation), which is consistent with the observation that MRSA pneumonia is not a mild disease. In hospital mortality was 7.7%, which was similar to a culture-based de-escalation strategy (Schlueter et al. Practice patterns for antibiotic de-escalation in culture-negative health care-associated pneumonia. *Infection.* 2010; 38:357–362).

### Use of Procalcitonin to Guide Duration of Antibiotics in Respiratory Infections

1. Schuetz et al. “Effect of procalcitonin-based guidelines vs standard guidelines on antibiotic use in lower respiratory tract infections: the ProHOSP randomized controlled trial.” *JAMA.* 2009;302(10):1059.
  - a. A multicenter, RCT in EDs of 6 tertiary care hospitals in Switzerland with an open intervention of 1359 patients with mostly **severe LRTIs** randomized between October 2006 and March 2008. INTERVENTION: Patients were randomized to administration of antibiotics based on a PCT algorithm or according to standard guidelines (control group). RESULTS: The rate of overall adverse outcomes was similar in the PCT and control groups. The mean duration of antibiotics exposure in the PCT vs control groups was lower in all patients (5.7 vs 8.7 days; 95% CI, -40.3% to -28.7%) and in the subgroups of patients with **CAP** (n = 925, **7.2 vs 10.7 days**; -32.4%; 95% CI, -37.6% to -26.9%), **AECOPD** (n = 228, **2.5 vs 5.1 days**; -50.4%; 95% CI, -64.0% to -34.0%), and **AECB** (n = 151, 1.0 vs 2.8 days; -65.0%; 95% CI, -84.7% to -37.5%). Antibiotic-associated adverse effects were less frequent in the PCT group (19.8% [n = 133] vs 28.1% [n = 193]; difference, -8.2%; 95% CI, -12.7% to -3.7%). Win-win for less side effects and less antibiotics.



2. Schuetz et al. “Excluding infection through procalcitonin testing improves outcomes of congestive heart failure patients presenting with acute respiratory symptoms: results from the randomized ProHOSP trial.” *Int J Carol* . 2014; 175(3):464-472.
  - a. A subgroup analysis of the heart failure patients from the ProHOSP trial (limited by being a post-hoc analysis) demonstrated that in patients with a low initial PCT (<0.25 ng/L) (n=60), those randomized to PCT guidance received fewer antibiotics and had fewer adverse outcomes (4% vs. 20%, p=0.01)(death/ICU admission) than those randomized to guideline treatment. This demonstrates the principle that “covering your bases” by treating patients for both volume overload and pneumonia can be dangerous to patients with pure cardiac pulmonary edema. This intuitively makes sense given QTc prolonging effects of azithromycin and flouroquinolones as well as the volume load associated with some beta-lactams.
3. Schuetz et al. “Procalcitonin to guide initiation and duration of antibiotic treatment in acute respiratory infections: an individual patient data meta-analysis.” *Clin Infect Dis*. 2012; 55(5):651.
  - a. A large meta-analysis of 14 randomized controlled trials specifically extracting patients with acute respiratory infections (a majority of patients in most trials). Most of the studies were conducted in Europe, with one having patients in the USA. The analysis showed that procalcitonin guided therapy was not associated with an increase in mortality or treatment failure in any clinical setting. This is some of the best data we have on anything in ID. 14 RCTs and counting, not including the more recent studies.
4. Branche et al. “Serum Procalcitonin Measurement and Viral Testing to Guide Antibiotic Use for Respiratory Infections in Hospitalized Adults: A Randomized Controlled Trial.” *J Infect Dis*. 2015;212:1692–1700
  - a. Branche et al conducted the first all-USA procalcitonin study, an RCT in adults hospitalized with non-pneumonic LRTI in New York. Inclusion criteria were adults  $\geq 21$  years of age with symptoms compatible with LRTI but without a definitive pneumonia on chest x-ray (“ambiguous findings”). They excluded all of the high-risk patients (sepsis, ICU admissions, etc), in order to demonstrate safety and efficacy in the “low-hanging fruit” of mild respiratory tract infections. They obtained 2 PCT levels and viral PCR testing at enrollment, and directed clinicians using the standard PCT algorithm: For PCT values of  $\leq 0.1$  ng/mL, initiation of antibiotic treatment is strongly discouraged; for values of 0.11–0.24 ng/mL, initiation is discouraged; for values of 0.25–0.49 ng/mL, initiation is encouraged; and for values of  $\geq 0.5$  ng/mL, initiation is strongly encouraged.” Results: Algorithm adherence was 64%. In low risk patients (**positive for virus and had a low PCT level**) there was a trend toward fewer days of antibiotics prescribed (median, 2 days [IQR, 1–6 days] vs 4 days [IQR, 0–8 days]; P = .11), with **significantly fewer patients discharged receiving antibiotics** (20% vs 45%; P = .002). Among subjects for whom treating physicians adhered to the algorithm (64%) revealed a significantly shorter duration of therapy, compared with the duration among nonintervention subjects (median, 2 days [IQR, 0–3 days] vs 4 days [IQR, 0–8 days]; P = .004).

## Appendix F: Tools for Running an Effective Meeting

### Tools for Establishing General Aims

TASK Establish general aims

General aim 1 \_\_\_\_\_  
\_\_\_\_\_

General aim 2 \_\_\_\_\_  
\_\_\_\_\_

General aim 3 \_\_\_\_\_  
\_\_\_\_\_

General aim 4 \_\_\_\_\_  
\_\_\_\_\_

Task assignment: \_\_\_\_\_ The Improvement Team \_\_\_\_\_

Due Date: \_\_\_\_\_ First team meeting \_\_\_\_\_

## Appendix G: Checklist for Core Elements of Hospital Antibiotic Stewardship Programs

Adapted from <http://www.cdc.gov/getsmart/healthcare/implementation/checklist.html>

For full explanations, please refer to the CDC Guide “Core Elements of Hospital Antibiotic Stewardship Programs” at <http://www.cdc.gov/getsmart/healthcare/pdfs/core-elements.pdf>

<b>Leadership support</b>	<b>Established at facility</b>	
Does your facility have a formal, written statement of support from leadership that supports efforts to improve antibiotic use (antibiotic stewardship)?	Yes	No
Does your facility receive any budgeted financial support for antibiotic stewardship activities (e.g., support for salary, training, or IT support)?	Yes	No

<b>Accountability</b>	<b>Established at facility</b>	
Is there a physician leader responsible for program outcomes of stewardship activities at your facility?	Yes	No

<b>Drug Expertise</b>	<b>Established at facility</b>	
Is there a pharmacist leader responsible for working to improve antibiotic use at your facility?	Yes	No

### Key support for the antibiotic stewardship program

<b><i>Does any of the staff below work with the stewardship leaders to improve antibiotic use?</i></b>	<b>Established at facility</b>	
Clinicians	Yes	No
Infection Prevention and Healthcare Epidemiology	Yes	No
Quality Improvement	Yes	No
Microbiology (Laboratory)	Yes	No
Information Technology (IT)	Yes	No
Nursing	Yes	No

**Actions to support optimal antibiotic use**

Policies	Policy established	
Does your facility have a policy that requires prescribers to document in the medical record or during order entry a dose, duration, and indication for all antibiotic prescriptions?	Yes	No
Does your facility have facility-specific treatment recommendations, based on national guidelines and local susceptibility, to assist with antibiotic selection for common clinical conditions?	Yes	No

**Specific interventions to improve antibiotic use**

Are the following actions to improve antibiotic prescribing conducted in your facility?  Broad interventions	Action performed	
Is there a formal procedure for all clinicians to review the appropriateness of all antibiotics 48 hours after the initial orders (e.g., antibiotic time out)?	Yes	No
Do specified antibiotic agents need to be approved by a physician or pharmacist prior to dispensing (i.e., pre-authorization) at your facility?	Yes	No
Does a physician or pharmacist review courses of therapy for specified antibiotic agents (i.e., prospective audit with feedback) at your facility?	Yes	No

**Pharmacy-driven interventions**

Are the following actions implemented in your facility?	Action performed	
Automatic changes from intravenous to oral antibiotic therapy in appropriate situations?	Yes	No
Dose adjustments in cases of organ dysfunction?	Yes	No
Dose optimization (pharmacokinetics/pharmacodynamics) to optimize the treatment of organisms with reduced susceptibility?	Yes	No
Automatic alerts in situations where therapy might be unnecessarily duplicative?	Yes	No
Time-sensitive automatic stop orders for specified antibiotic prescriptions?	Yes	No

**Diagnosis and infections specific interventions**

Does your facility have specific interventions in place to ensure optimal use of antibiotics to treat the following common infections?	Action performed	
Community-acquired pneumonia	Yes	No
Urinary tract infection	Yes	No
Skin and soft tissue infections	Yes	No
Surgical prophylaxis	Yes	No
Empiric treatment of Methicillin-resistant <i>Staphylococcus aureus</i> (MRSA)	Yes	No
Non- <i>C. Difficile</i> infection (CDI) antibiotics in new cases of CDI	Yes	No
Culture-proven invasive (e.g., blood stream) infections	Yes	No

**Tracking: Monitoring antibiotic prescribing, use, and resistance**

Process measures	Measure performed	
Does your stewardship program monitor adherence to a documentation policy (dose, duration, and indication)?	Yes	No
Does your stewardship program monitor adherence to facility-specific treatment recommendations?	Yes	No
Does your stewardship program monitor compliance with one of more of the specific interventions in place?	Yes	No

Antibiotic use and outcome measures	Measure performed	
Does your facility track rates of <i>C. difficile</i> infection?	Yes	No
Does your facility produce an antibiogram (cumulative antibiotic susceptibility report)?	Yes	No

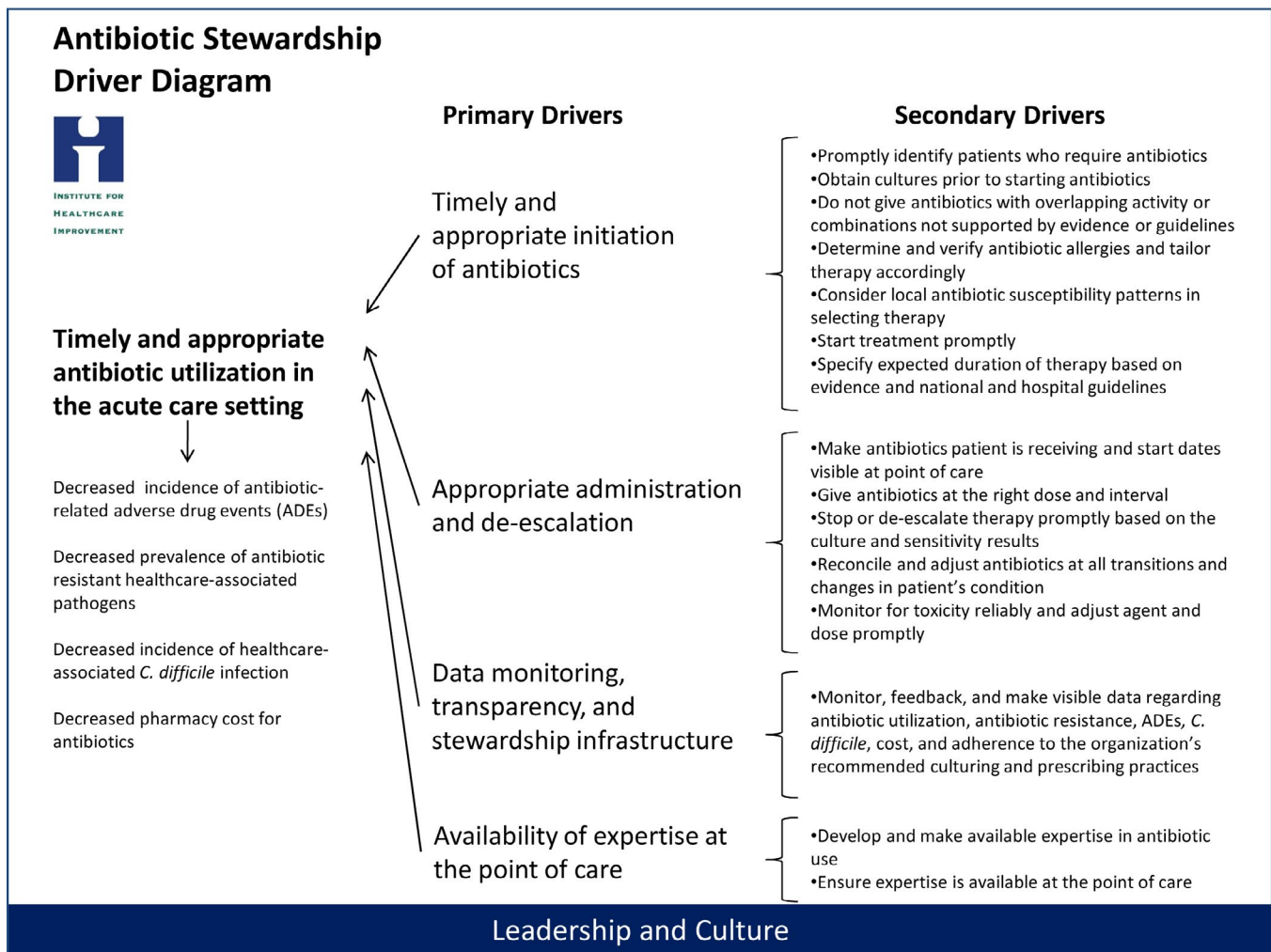
Does your facility monitor antibiotic use (consumption) at the unit and/or facility wide level by one of the following metrics:	Measure performed	
By counts of antibiotic(s) administered to patients per day (Days of Therapy; DOT)?	Yes	No
By number of grams of antibiotics used (Defined Daily Dose, DDD)?	Yes	No
By direct expenditure for antibiotics (purchasing costs)?	Yes	No

Reporting information to staff on improving antibiotic use and resistance	Measure performed	
Does your stewardship program share facility-specific reports on antibiotic use with prescribers?	Yes	No
Has a current antibiogram been distributed to prescribers at your facility?	Yes	No
Do prescribers ever receive direct, personalized communication about how they can improve their antibiotic prescribing?	Yes	No

Education	Measure performed	
Does your stewardship program provide education to clinicians and other relevant staff on improving antibiotic prescribing?	Yes	No

## Appendix H: CDC/IHI Driver Diagram (Reproduced with permission from the CDC)

### Antibiotic Stewardship Driver Diagram



## Appendix I: Online Resources for Provider Education on Antibiotic Stewardship

Four one-hour online modules will be provided to teams participating in Project STEP IN:

- Introduction to Antibiotic Stewardship for Hospitalists
- A Stewardship Approach to Pneumonia
- A Stewardship Approach to Skin and Soft Tissue Infections and *Staphylococcus aureus* Infections
- A Stewardship Approach to Urinary Tract Infections

In addition to these modules, there are numerous stewardship education resources online. The following are recommended for physicians, from a review by Drs. Ohl and Luther<sup>1</sup>:

- An Antibiotic Stewardship Curriculum for Medical Students
  - (Great curriculum, applicable to inpatient prescribers)
  - <http://www.wakehealth.edu/School/CAUSE/Get-Smart-About-Antibiotics.htm>
- Prudent Antibiotic User (PAUSE)
  - (Requires account creation – great curriculum for medical residents, applies to inpatient physicians as well)
  - <http://www.pause-online.org.uk>
- Scottish Antimicrobial Prescribing Group (for Primary Care Providers)
  - <http://www.scottishmedicines.org.uk/SAPG/Education/Education>
- Get Smart About Antibiotics (CDC) for healthcare professionals:
  - <http://www.cdc.gov/getsmart/specific-groups/hcp/index.html>
- Stanford Online course: Antimicrobial Stewardship: Optimization of Antibiotic Practices (CME) (mainly for outpatient providers)
  - <http://online.stanford.edu/course/antimicrobial-stewardship-optimization-antibioticpractices>
- World Health Organization Good Prescribing Guide
  - Generic principles of clinical pharmacology, but has relevance to stewardship – See the Process of Rational Prescribing (p.11 in the PDF)
  - <http://apps.who.int/medicinedocs/en/d/Jwhozip23e/>

An entire issue supplemental issue of the *Journal of Hospital Medicine* was devoted to antimicrobial stewardship and serves as an excellent basis for provider education. See references for article topics.<sup>2-6</sup>



## References

1. Ohl CA, Luther VP. Health care provider education as a tool to enhance antibiotic stewardship practices. *Infect Dis Clin North Am.* 2014;28(2):177-193.
2. File TM, Jr. Duration and cessation of antimicrobial treatment. *J Hosp Med.* 2012;7 Suppl 1:S22-33.
3. Kaye KS. Antimicrobial de-escalation strategies in hospitalized patients with pneumonia, intra-abdominal infections, and bacteremia. *J Hosp Med.* 2012;7 Suppl 1:S13-21.
4. Rosenberg DJ. Infections, bacterial resistance, and antimicrobial stewardship: the emerging role of hospitalists. *J Hosp Med.* 2012;7 Suppl 1:S34-43.
5. Rosenberg DJ. Key aspects of antimicrobial stewardship. *J Hosp Med.* 2012;7 Suppl 1:S1.
6. Snyderman DR. Empiric antibiotic selection strategies for healthcare-associated pneumonia, intra-abdominal infections, and catheter-associated bacteremia. *J Hosp Med.* 2012;7 Suppl 1:S2-12.

## Appendix J: Establish General Aims

Establishing good goals is essential for maintaining focus and motivating the team.

Eventually your aims should be specific, measurable and time-defined and should specify the population or populations for whom you want to improve care. A “stretch” goal should be established that should be aggressive enough to mandate a change in the design of your current process in order to achieve it. Until you have reliable metrics and a baseline evaluation, however, team-supported general aims or goals can be important for galvanizing action and establishing clarity of purpose.

One important task is to define the scope of your efforts. Do you want to focus on just one ward or service? On just one group of physicians? For a one-month or three-month period? Again, a broad view of the scope of your efforts is encouraged as affecting all inpatients with heart failure, but it may be reasonable to start small and then spread your improvement methods to other areas. On the other hand, even if the scope of your effort includes all patients in your hospital or system, the interventions you choose should be piloted on a small scale when possible. The bottom line is this: think BIG! Initially, don't bite off more than you can chew, but serial testing and learning on a small scale can make even very large projects more manageable.

### Examples of General Aims

1. General Aim 1: Substantially improve pneumonia care for hospitalized patients.
2. General Aim 2: Decrease pneumonia readmissions.
3. General Aim 3: Improve pneumonia core measures.
4. General Aim 4: Increase the knowledge of caregivers about taking care of hospitalized pneumonia patients.

As your team develops, your challenge will be to define many of the terms in your general aims, which will entail developing defined metrics and more mature, specific, time-defined aims. For example, what aspects of pneumonia care do you want to improve first? What are the factors that lead to readmission? Which of the pneumonia core measures needs the most improvement? How do we educate caregivers about pneumonia care?

### **TASK: Establish General Aims.**

General Aim 1 \_\_\_\_\_

General Aim 2 \_\_\_\_\_

General Aim 3 \_\_\_\_\_

General Aim 4 \_\_\_\_\_

**Task Assignment:** The Improvement Team

**Due Date:** First team meeting

## Appendix K: Sample Drug Use Evaluation

Adapted from SHEA Drug Use Evaluation form: <https://www.shea-online.org/priority-topics/antimicrobial-stewardship/implementation-tools-resources>

[Hospital Name]

Drug Use Evaluation

**Title:** An Evaluation of Piperacillin-tazobactam Use in Adult Inpatients on the Hospitalist Service

**Project Committee:** [Team members]

**Research Question:** How is piperacillin/tazobactam being utilized in the adult inpatients on the hospitalist service at our hospital?

### Background

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Piperacillin/tazobactam is a parenteral  $\beta$ -lactam/ $\beta$ -lactamase inhibitor combination that demonstrates in vitro activity against a broad spectrum of gram-positive, gram-negative, aerobic and anaerobic strains of bacteria, including methicillin-sensitive *S. aureus*, *S. epidermidis*, *S. pneumoniae*, *E. faecalis*, *E. faecium*, *H. influenzae*, *M. catarrhalis*, *E. coli*, *E. cloacae*, *E. aerogenes*, *C. diversus*, *C. freundii*, *M. morgani*, *K. pneumoniae*, *K. oxytoca*, *N. meningitidis*, *S. marcescens*, *P. mirabilis*, *P. vulgaris*, *P. aeruginosa*, *S. maltophilia*, *Acinetobacter* spp., and *Bacteroides* spp. Piperacillin inhibits bacterial cell wall synthesis by binding to penicillin-binding proteins. Tazobactam inhibits a wide variety of bacterial  $\beta$ -lactamases by irreversibly binding to the enzyme's catalytic site. This prevents hydrolytic action on piperacillin's  $\beta$ -lactam ring and increases piperacillin's antibacterial activity. Piperacillin is effective against most gram-positive organisms such as *S. pneumoniae*, and gram-negative organisms including *Pseudomonas* spp. The addition of tazobactam broadens the coverage of the antibiotic combination to include anaerobic bacteria and other pathogens that commonly produce  $\beta$ -lactamases such as *E. coli* and *K. pneumoniae*. This combination is particularly useful for empiric treatment of polymicrobial infections such as complicated intra-abdominal infections, diabetic foot infections, and other infections that require broad empiric coverage.

Piperacillin/tazobactam has good penetration into the lungs, intestinal mucosa, skin, muscle, uterus, ovary, prostate, gall bladder, and bile, but has poor CSF penetration. It has a half-life of ~ 1 hour. Both piperacillin and tazobactam are renally eliminated, with ~ 20% of piperacillin being eliminated in the feces. The recommended adult dosage at the XX hospital in patients with normal renal function is 3.375 g to 4.5 g every 6 hours. In patients with CrCl 20-40 mL/min, the dose should be reduced to 2.25 g every 6 hours (3.375 g every 6 hours for Pseudomonal infections). In patients with CrCl < 20 mL/min, the dose should be reduced to 2.25 g every 8 hours (2.25 g every 6 hours for Pseudomonal infections). In patients undergoing intermittent hemodialysis, the dose should be reduced to 2.5 g every 12 hours (2.25 g every 8 hours for Pseudomonal infections). Common adverse drug reactions related to piperacillin/tazobactam use include diarrhea, constipation, nausea, vomiting, headache, and hypersensitivity reactions. Serious, but rare, adverse effects such as agranulocytosis, interstitial nephritis and Stevens-Johnson Syndrome have been reported.

At our hospital, piperacillin/tazobactam is a formulary agent.

## Objectives

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1. To describe indications for the use of piperacillin/tazobactam in adult inpatients on the hospitalist service.
2. To evaluate the appropriateness of piperacillin/tazobactam indication, dosing, and duration of therapy.
3. To estimate the incidence of adverse events directly associated with piperacillin/tazobactam.

## Methods

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### Study Design

A retrospective chart review will be conducted to include adult inpatients on the hospitalist service receiving piperacillin/tazobactam between January 1, 2016 and July 31, 2016.

Data will be collected using a data collection form, and all patient identifiers will be de-identified. All collected patient data, including demographic data, antibiotic regimens, microbiology data, indications, etc., will be analyzed.

### Inclusion Criteria

Adult inpatients who received piperacillin/tazobactam between January 1, 2016 and July 31, 2016 for a total target sample size of 100 patients.

### Exclusion Criteria

- Oncology patients
- Piperacillin/tazobactam course duration <24 hours.

### Data Collection

Patient demographics, antibiotic regimens and dosing, indication for piperacillin/tazobactam use, radiographic data, microbiological data and adverse events will be collected from pharmacy order entry system, computerized physician order entry system, electronic patient record, and patient's paper chart.

### Data Collection Endpoints:

Data will be collected until discontinuation of piperacillin/tazobactam, patient discharge from the hospital or patient death.

## Definitions

Empiric therapy: antibiotic therapy initiated prior to the first positive culture

Directed therapy: antibiotic therapy directed at final organisms

One piperacillin/tazobactam treatment course: a dose at least 24 hours apart for a duration of at least 24 hours

Concomitant antimicrobials: antibiotics administered for at least 24 hours while simultaneously receiving piperacillin/tazobactam

## Statistical Analysis

Descriptive statistics will be used to describe the endpoints listed above.

Unit of analysis: one course of piperacillin/tazobactam therapy

## Results

Table IA: General Patient Demographics (n=100)

Antibiotic Allergies, N (%)		Patient's Age (years)		Gender, N (%)	
Penicillin		Mean		Female	
Cephalosporin		Median		Male	
Carbapenem		Range			
Other antibiotics					

Table IB: Breakdown of Piperacillin/Tazobactam Courses by Location

Courses, n(%)					
Floor		ICU		Step-down	

Table IIA: Initiation of Therapy

Courses, n (%) N=XX	
Empiric	
Directed	

Table IIB: Indications for Piperacillin/Tazobactam Therapy

Indication (N=XX)	N (%)	Empiric vs. directed, n (%)
Pulmonary		
Total cultures (sputum, BAL, nasotracheal aspirate)		
Intra-abdominal		
Total cultures (bile, abdominal abscess, peritoneal fluid)		
Skin and soft tissue		
Total cultures		
Urinary Tract Infection		
Total cultures		
Fever of Unknown Origin		
Total cultures (blood, urine)		

Table IIC: Reason for Discontinuation of Piperacillin/Tazobactam Therapy

No. of Piperacillin/Tazobactam Courses, N=XX	n (%)
Completed course	
Changed to oral therapy	
Changed to narrower agent	
Organism resistant	
Patient expired	
Patient discharged home on piperacillin/tazobactam	
Culture negative/Other	

Table IIIA: Dosing Based on Renal Function

<b>Piperacillin/Tazobactam Initial Regimen</b>	<b>No. of Piperacillin/Tazobactam Courses, n (%) N=XX</b>
Appropriate	
Inappropriate	
Under-dose	
Over-dose	
<b>Piperacillin/Tazobactam Subsequent Regimen</b>	<b>No. of Subsequent Piperacillin/Tazobactam, n (%) N=XX</b>
Appropriate	
Inappropriate	
Under-dose	
Over-dose	

## IV. Duration of Piperacillin/Tazobactam Therapy

**Table IVA:** Duration of Piperacillin/Tazobactam Therapy

<b>Duration of Treatment</b>	<b>No. of Piperacillin/Tazobactam Courses, n (%) N=XX</b>	<b>Empiric vs. Directed, n</b>
1-3 days		
4-7 days		
8-10 days		
11-14 days		
>14 days		

## V. Concomitant Antimicrobials

Table VA: Concomitant Antibiotics (administered for at least 24 hours while simultaneously receiving piperacillin/tazobactam)

<b>Agent</b>	<b>Number of Courses, n (%) N=XX</b>

## VI. Piperacillin/Tazobactam-Related Adverse Effects

Summarize any piperacillin/tazobactam related adverse events here.

## Conclusions

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Place your conclusions of the study results here. Make it simple and brief.

### Recommendations

Recommendations should be very specific and should include ideas on how to improve problematic use of antimicrobial identified in this DUE.

- Restrict a piperacillin/tazobactam to Infectious Diseases prior approval
- Routine review of all piperacillin/tazobactam orders at 72 hours or automatic stop orders
- Development of piperacillin/tazobactam guidelines
- Development of the piperacillin orderset
- Education

## Limitations

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State limitations of the study here.

## References

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1. Johnson CA, Halstenson CE, Kelloway JS, et al. Single-dose pharmacokinetics of piperacillin and tazobactam in patients with renal disease. *Clin Pharmacol Ther.* 1992;51:32-41.
2. Schoonover LL, Occhipinti DJ, Rodvold KA, et al. Piperacillin/tazobactam: A new beta-lactam/beta-lactamase inhibitor combination. *Ann Pharmacother.* 1995;29:501-514.



## Appendix L: UTI Definitions and Algorithm

**Table 1** illustrates why many people are confused about the definition of a UTI. National societies have published numerous lists of urinary tract symptoms that qualify for treatment, based on inclusion and exclusion criteria from published studies. Many of these lists require combinations of criteria, such as fever + localizing symptoms, or leukocytosis + localizing symptoms, or 2 or more localizing symptoms in the absence of fever, etc. The one list which has an excellent evidence base (studied in a cluster-randomized trial at 12 nursing homes in Canada), is the Loeb criteria. The Loeb algorithm actually starts with fever and then asks how likely the fever is to be coming from another source. Using their algorithm with provider education, they decreased antibiotic use for UTIs (though overall antibiotic use did not change) without an increase in hospital admissions or mortality. The Loeb criteria are incorporated into the Stone criteria. Most of these criteria have been studied in long-term care. The IDSA CAUTI criteria have been used by Dr. Trautner in 2 prospective stewardship interventions in hospitalized patients.<sup>2,3</sup>

**Figure 1** is a tool developed by the Colorado Hospital Association's Antimicrobial Stewardship Collaborative which includes Barbara Trautner, MD, PhD, one of the nation's leading experts on UTI; Heidi Wald, MD, MPH, a Geriatrician and Vice Chair of Quality at the University of Colorado; and Arjun Srinivasan, MD, CAPT, from the CDC. This algorithm represents a "common sense" approach to urinary tract infections and is highly usable by clinicians. Though it has not been validated in any clinical trials to date, the individual components are derived from national guidelines. Thanks to the members of the Colorado Hospital Association, Teri Hulett, RN, BSN, CIC, FAPIC, and Sara Hodgson, MS, for letting us use this tool.

Table 1. UTI Criteria from published guidelines

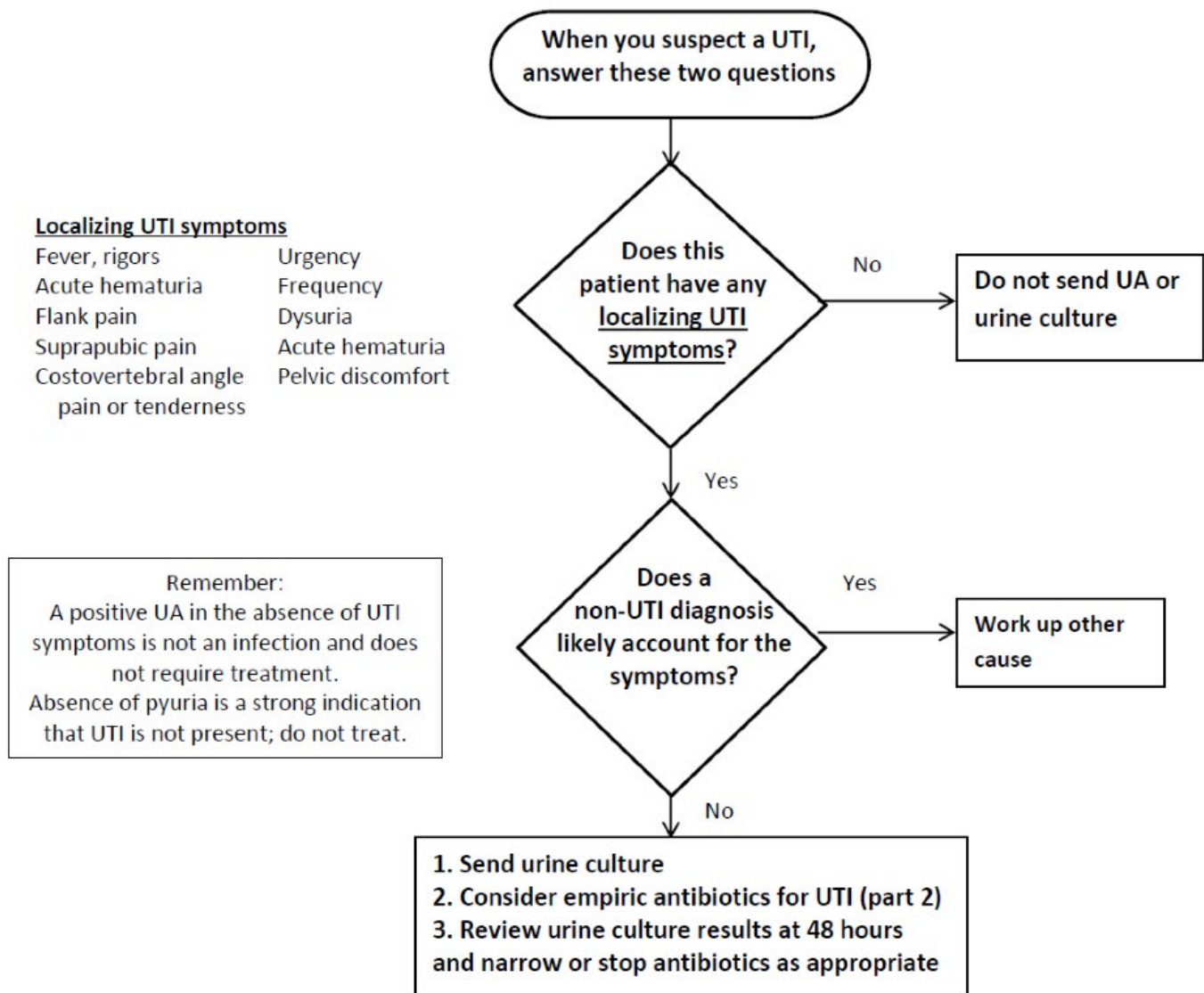
	IDSA Guidelines on ASB, 2005 <sup>4</sup>	IDSA Guidelines for Cystitis/Pyelo in women, 1999 <sup>5</sup>	IDSA Guidelines for CAUTI, 2009 <sup>6</sup>	NIDRR 1992 <sup>7</sup>	Loeb (SHEA) Criteria, 2001 <sup>8</sup>	Stone (Revised McGeer) Criteria for UTI, 2012 <sup>9</sup>	NHSN Surveillance Definition for CAUTI, 2009 <sup>10</sup>
Catheterized patients							
New onset fever >38C, or provider report of fever			X	X	X	X	X
Rigors			X		X	X	
AMS without alternative cause			X		X	X	
Suprapubic pain or tenderness			X	X	X	X	X
Acute hematuria			X		X	X	
Costovertebral pain or tenderness			X	X	X	X	X
Increased spasticity or autonomic dysreflexia in patients with SCI			X	X			
Urinary catheter removed in <48 hours							
Any of the above criteria OR							
Urgency			X				X
Frequency			X				X
Dysuria			X				X
No history of urinary catheter or removal in >48 hours prior to symptom onset							
Fever >38C without other cause	X	X			X	X	X
Urgency	X	X			X	X	X
Frequency	X	X			X	X	X
Dysuria	X	X			X	X	X
Costovertebral pain or tenderness/ flank pain	X	X			X	X	X
Suprapubic pain or tenderness	X				X	X	X
Acute hematuria					X	X	
New or worsening incontinence					X	X	
Rigors/hypotension/leukocytosis without another cause					X	X	

IDSA: Infectious Diseases Society of America; ASB: asymptomatic bacteriuria; CAUTI: catheter-associated urinary tract infection; NIDRR: National Institute on Disability and Rehabilitation Research; NSHN: National Healthcare Safety Network

Figure 1. Colorado Hospital Association Guideline for UTI Diagnosis<sup>1</sup>

**4 Key concepts to optimize diagnosis of UTI in hospitalized patients:**

- 1) Most UTIs present with fever and/or symptoms localizing to the urinary tract.
- 2) Antibiotics are not recommended to treat colonization of the urinary tract (asymptomatic bacteriuria), except in pregnancy and invasive genitourinary procedures.
- 3) Urinalysis and urine culture have poor test characteristics in older patients and patients with indwelling urinary catheters—they should not be sent unless symptoms are present.
- 4) Alteration in mental status (delirium) is neither sensitive nor specific for UTI. Thus delirium without other localizing symptoms is unlikely to be a UTI.



This is intended as a guide for evidence-based decision-making and should not replace clinical judgement.

References: Trautner BW, Grigoryan L, Petersen NJ, et al. *JAMA Intern Med.* Published online May 26, 2015; IDSA Guideline for ABU 2005; IDSA Guideline for CAUTI 2009

## References

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## Appendix M1: Surveillance Form: Appropriateness of Urine Culture Ordering and UTI Treatment – CDC

### Assessment of Appropriateness of Antibiotics for Urinary Tract Infections (UTIs)

1. Date: \_\_\_\_\_ Gender:      Male    Female  
Age: \_\_\_\_\_ Service: \_\_\_\_\_

2. Did the patient have a urinary catheter in place at the time of diagnosis or in the 48h preceding diagnosis?  
\_\_\_\_\_ Yes      \_\_\_\_\_ No

3. Does the patient have any of the following underlying comorbidities? (Check all that apply)

\_\_\_ kidney stones                      \_\_\_ urologic abnormality  
\_\_\_ pregnancy                         \_\_\_ neutropenia  
\_\_\_ history of renal transplant

4. Were any of the following signs or symptoms documented? (Check all that apply)

\_\_\_ dysuria                                \_\_\_ flank pain  
\_\_\_ urgency                                \_\_\_ fever (>38°C) or rigors  
\_\_\_ frequency                              \_\_\_ WBC >11,000 cells/μL  
\_\_\_ suprapubic pain                        \_\_\_ nausea and/or vomiting  
\_\_\_ new onset delirium\*                    \_\_\_ other (please document below)

(\*Criteria should not be used alone. Should be taken into account with other signs and symptoms)

5. Was a urinalysis sent?                      \_\_\_\_\_ Yes      \_\_\_\_\_ No

A. If Yes, was there evidence of pyuria (> 5-10 WBCs/high power field)?                      \_\_\_\_\_ Yes      \_\_\_\_\_ No

B. If Yes, were epithelial cells noted? (please specify number/high power field)                      \_\_\_\_\_ Yes      \_\_\_\_\_ No

C. If dipstick results available, were either of the following detected? (Check all that apply)

\_\_\_ leukocyte esterase                      \_\_\_ nitrites

6. Was a urine culture sent?  Yes  No  
 A. If Yes, was the urine culture positive?  Yes  No  
 B. If culture was positive, document the organism(s) and colony count(s):  Yes  No
- 

7. If a urinalysis and/or urine culture were collected, please designate how urine was collected:

- Clean catch  
 Indwelling catheter  
 Straight catheterization  
 Collection method not specified

8. Was the patient receiving antibiotics prior to collection of the urine culture?  Yes  No

9. Were empiric antibiotics (started prior to culture results) consistent with institutional/national guidelines? (Document antibiotic below)  Yes  No

---

10. Was the urinary catheter removed after a diagnosis of CA-UTI or catheter-associated asymptomatic bacteriuria (CA-ASB)?  Yes  No

A. If **Not**, was a reason for continuation documented? (Please specify below)

---

11. Were empiric antibiotics stopped if no organism was isolated by culture?  Yes  No

A. If **No**, was an indication for continued antibiotics documented?

Please specify indication for continuation: \_\_\_\_\_

12. If an organism was isolated by culture, was it susceptible to the prescribed antibiotic? (**PRINT ANTIBIOTIC SUSCEPTIBILITY REPORT**)  Yes  No

13. Were antibiotics changed after culture results were available?  Yes  No

A. If YES, please document antibiotic change:

---

14. Total duration of antibiotic therapy for UTI while an inpatient?

Days

15. Was an ID consult team involved the patient's care?  Yes  No

## Appendix M2: UTI Scoring Assessment: Appropriateness of Urine Culture Ordering and Treatment Rates of Asymptomatic Bacteriuria

Use the CDC Tool [Assessment of Appropriateness of Antibiotics for Urinary Tract Infections (UTIs)] to review the charts of 50 patients on the hospitalist service who received antibiotics for a UTI in a designated time period.

Exclude patients with any of the conditions in Q3 from data reporting.

Metric	Number of patients	% Appropriate
<b>CLINICAL CRITERIA</b>		
How many patients in the sample had at least 1 listed criteria in Q4? (or 2 in the case of delirium)		
Catheter present		
No catheter present		
TOTAL: Symptomatic UTI		
TOTAL: Asymptomatic bacteriuria		
<b>LAB CRITERIA</b>		
How many patients had a UA sent?		
How many patients had pyuria?		
What percentage were contaminated with epithelial cells? (poor collection)		
What percentage had a urine culture sent?		
What percentage met microbiologic criteria for a UTI?		
<b>ANTIBIOTIC USE</b>		
What was the total number of antibiotic days given in the sample?		
TOTAL: Symptomatic UTI		
TOTAL: Asymptomatic bacteriuria		
What was the mean duration of antibiotics (inpatient + outpatient) in the sample?		
TOTAL: Symptomatic UTI		
TOTAL: Asymptomatic bacteriuria		
What percentage of courses were concordant with local/national guidelines?		

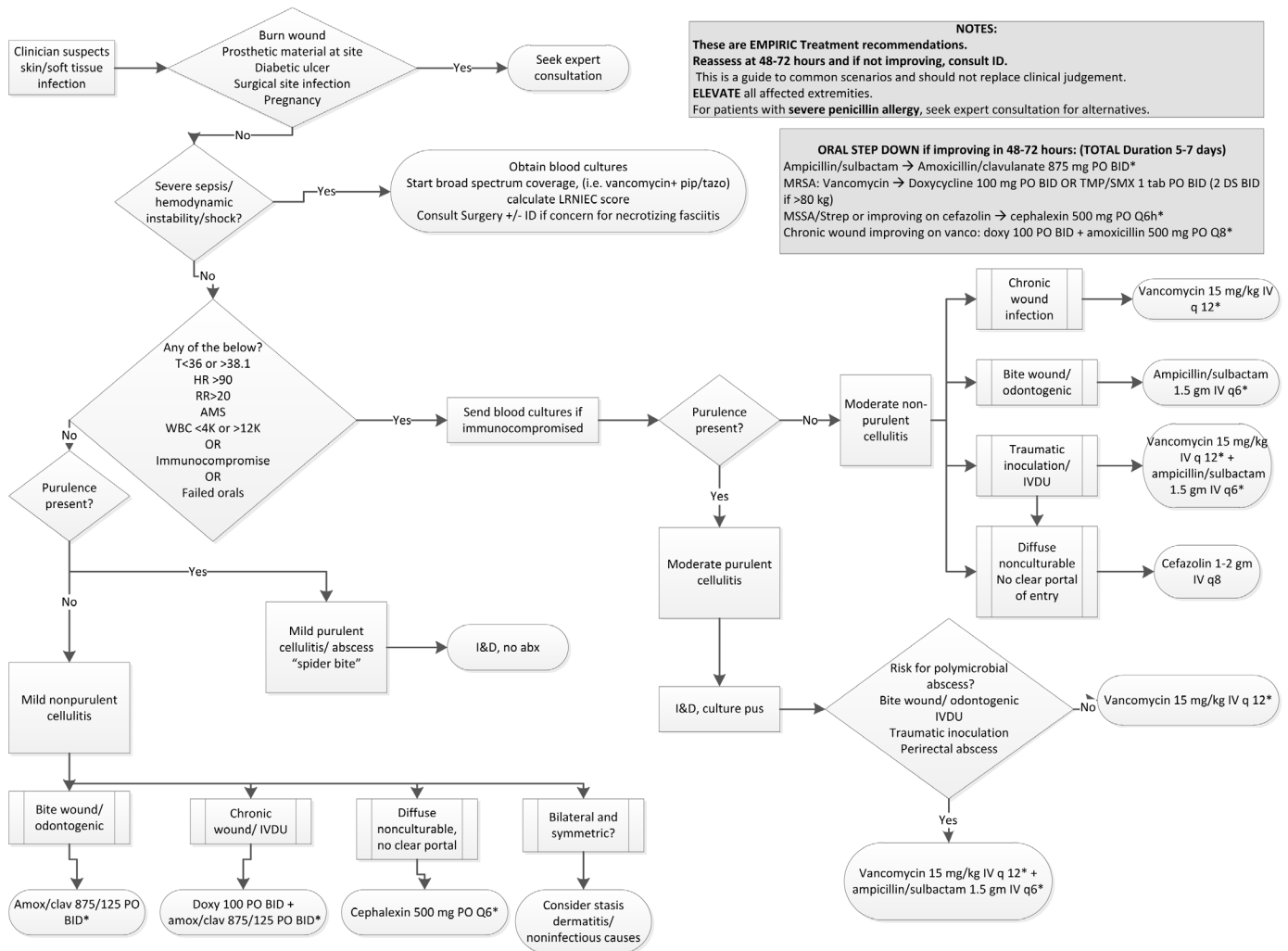


## Appendix N: ICD-9/ICD-10 Codes for Infections in Hospitalized patients

Below are the umbrella categories for ICD-9 and ICD-10 codes. If your hospital is interested in doing detailed case reviews and you would like a complete listing, please contact the Society of Hospital Medicine at [thecenter@hospitalmedicine.org](mailto:thecenter@hospitalmedicine.org).

ICD-9 CODE	ICD-9 CODE DESCRIPTION	ICD-10 CODE	ICD-10 CODE DESCRIPTION
<b>Pneumonia</b>			
480	Viral pneumonia	J12	Viral pneumonia, not elsewhere classified
481	Pneumococcal pneumonia [ <i>Streptococcus pneumoniae pneumonia</i> ]	J13	Pneumonia due to <i>Streptococcus pneumoniae</i>
482	Other bacterial pneumonia	J14	Pneumonia due to <i>Hemophilus influenzae</i>
483	Pneumonia due to other specified organism	J15	Bacterial pneumonia, not elsewhere classified
484	Pneumonia in infectious diseases classified elsewhere	J16	Pneumonia due to other infectious organisms, not elsewhere classified
485	Bronchopneumonia, organism unspecified	J17	Pneumonia in diseases classified elsewhere
486	Pneumonia, organism unspecified	J18	Pneumonia, unspecified organism
<b>Urinary Infections</b>			
590	Infections of the kidney	N10 N11.9 N12 N13.6	Acute tubulo-interstitial nephritis; Chronic tubule-interstitial nephritis; Tubulo-interstitial nephritis, not specified Pyonephrosis
595	Cystitis	N30	Cystitis
599	Urinary tract infection, site not specified	N39	UTI, site not specified
<b>Skin and soft tissue infections</b>			
680	Carbuncle and furuncle	L02	Cutaneous abscess, furuncle and carbuncle
681	Cellulitis and abscess of finger and toe	L03	Cellulitis and acute lymphangitis
682	Other cellulitis and abscess	L04	Acute lymphadenitis
686	Other local infections of skin and subcutaneous tissue	L08	Other local infections of skin and subcutaneous tissue

## Appendix O: SSTI Algorithm short



**NOTES:**  
 These are **EMPIRIC Treatment recommendations**.  
**Reassess at 48-72 hours and if not improving, consult ID.**  
 This is a guide to common scenarios and should not replace clinical judgement.  
**ELEVATE** all affected extremities.  
 For patients with **severe penicillin allergy**, seek expert consultation for alternatives.

**ORAL STEP DOWN if improving in 48-72 hours: (TOTAL Duration 5-7 days)**  
 Ampicillin/sulbactam → Amoxicillin/clavulanate 875 mg PO BID\*  
 MRSA: Vancomycin → Doxycycline 100 mg PO BID OR TMP/SMX 1 tab PO BID (2 DS BID if >80 kg)  
 MSSA/Strep or improving on cefazolin → cephalexin 500 mg PO Q6h\*  
 Chronic wound improving on vanco: doxy 100 PO BID + amoxicillin 500 mg PO Q8\*

\*Needs adjustment for abnormal renal function, consult pharmacy

## Appendix P: Part - 1 SSTI Assessment

### Assessment of Appropriateness of Antibiotics for Skin and Soft Tissue Infections (SSTI's)

1. Date: \_\_\_\_\_ Gender: Male Female  
Age: \_\_\_\_\_ Service: \_\_\_\_\_
2. Did the patient have documented evidence of a severe/deep infection at diagnosis? (Check all that apply)
- Hypotension (SBP<90)       Crepitus  
 Bullae       End organ dysfunction (oliguria/AKI)  
 skin sloughing       bone or tendon infection  
 myositis       ICU admission  
 2 or more SIRS Criteria
3. Did the patient have any of the following underlying comorbidities? (Check all that apply)
- HIV/AIDS       Diabetes with A1c >8  
 Neutropenia (ANC <500)       Chronic steroid use  
 Organ transplantation       Cirrhosis  
 Malignancy on chemotherapy       Other immunosuppressive use
4. Were any of the following complicating factors documented? (Check all that apply)
- chronic wound       prosthetic material at site  
 bite (animal or human)       lymphedema  
 ischemic limb/gangrene       recurrent cellulitis  
 surgical site infection       burn wound  
 tooth infection       facial/genito-rectal cellulitis  
 Injection drug use (IVDU)
5. Was purulence noted? (Abscess or purulent drainage) \_\_\_\_\_ Yes \_\_\_\_\_ No
- A. If Yes, was drainage performed? \_\_\_\_\_ Yes \_\_\_\_\_ No
- B. If Yes, were cultures sent from the drainage? \_\_\_\_\_ Yes \_\_\_\_\_ No

6. Were any other cultures sent? \_\_\_\_\_ Yes      \_\_\_\_\_ No

    \_\_\_\_\_ Wound swab

    \_\_\_\_\_ Blood cultures

    \_\_\_\_\_ Other \_\_\_\_\_

7. Were empiric antibiotics (started prior to culture results) consistent with institutional/national guidelines? (Document antibiotic below) \_\_\_\_\_ Yes      \_\_\_\_\_ No

\_\_\_\_\_

8. Was the leg elevated?

    A. If **Not**, was a reason for not elevating documented? (Please specify below) \_\_\_\_\_ Yes      \_\_\_\_\_ No

    \_\_\_\_\_

9. Was the patient improving at 72 hours? \_\_\_\_\_ Yes      \_\_\_\_\_ No

    A. If **No**, was any additional workup done? \_\_\_\_\_ Yes      \_\_\_\_\_ No

    Please specify: \_\_\_\_\_

    B. If yes, were antibiotics narrowed or changed to oral? \_\_\_\_\_ Yes      \_\_\_\_\_ No

10. If an organism was isolated by culture, was it susceptible to the prescribed antibiotic? \_\_\_\_\_ Yes      \_\_\_\_\_ No

**(PRINT ANTIBIOTIC SUSCEPTIBILITY REPORT)**

11. Were antibiotics changed after culture results were available? \_\_\_\_\_ Yes      \_\_\_\_\_ No

    A. If YES, please document antibiotic change:

    \_\_\_\_\_

12. Total duration of antibiotic therapy for SSTI while an inpatient?

    \_\_\_\_\_ Days

13. Was an ID consult team involved the patient's care?

\_\_\_\_\_ Yes

\_\_\_\_\_ No

## Appendix P: Part 2 - SSTI Score Card

Review the charts according to the above checklist and total the following responses.

- 1) Summarize the complicated cases including patients with criteria mentioned in Q2 (severe infections), Q3 (immunocompromised patients) and Q4 (complicating factors). These patients often meet criteria for broader spectrum therapy.

Management of SSTIs			
	Number of patients	Appropriate management	% Appropriate
<b>Purulent Cellulitis</b>			
Incision and drainage performed		Yes	
Abscess cultures obtained		Yes	
Empiric abx consistent with guidelines		Yes	
Improvement at 72 hours		Yes	
Antibiotics modified for culture		Yes	
Vancomycin use		Yes	
Broad-spectrum GNR use*		Case-dependent (See algorithm)	
Duration of IV therapy		7–14 days	
Total duration of abx		7–14 days	
Infectious Disease consultation		Yes	
<b>Non-Purulent Cellulitis</b>			
Wound swab performed		No	
Empiric abx consistent with guidelines		Yes	
Improvement at 72 hours		Yes	
Vancomycin use		Case-dependent	
Broad-spectrum GNR use*		Case-dependent	
Duration of IV therapy		7–14 days	
Total duration of abx		7–14 days	
ID consultation		Yes	

\* GNR = gram-negative rod. Drugs with broad spectrum GNR coverage include ceftriaxone, cefepime, piperacillin/tazobactam, meropenem, imipenem, ertapenem, aztreonam, ciprofloxacin, levofloxacin

2) Exclude patients with any of the conditions listed in Question 2, 3 or 4 from the analysis.

Management of Complicated SSTI				
	Number of patients	%	Appropriate management	% Appropriate
<b>Purulent Cellulitis</b>				
Incision and drainage performed			Yes	
Abscess cultures obtained			Yes	
Empiric abx consistent with guidelines			Yes	
Improvement at 72 hours			Yes	
Antibiotics modified for culture			Yes	
Vancomycin use			Yes	
Broad-spectrum GNR use*			No	
Duration of IV therapy			3–5 days	
Total duration of abx			5–7 days	
Infectious disease consultation			Case-dependent	
<b>Non-Purulent Cellulitis</b>				
Wound swab performed			No	
Empiric abx consistent with guidelines			Yes	
Improvement at 72 hours			Yes	
Vancomycin use			No	
Broad-spectrum GNR use*			No	
Duration of IV therapy			3–5 days	
Total duration of abx			5–7 days	
ID consultation			Case-dependent	

\* GNR = gram-negative rod. Drugs with broad GNR coverage include ceftriaxone, cefepime, piperacillin/tazobactam, meropenem, imipenem, ertapenem, aztreonam, ciprofloxacin, levofloxacin

## Appendix Q1 - Assessment of Appropriateness of Antibiotics for Community-Acquired Pneumonia (CAP)

### Definition

- |  |                              |                             |
|--|------------------------------|-----------------------------|
| 1. Was the patient hospitalized in an acute care hospital for >2 days within 90 days of the diagnosis of pneumonia?  | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| 2. Did the patient reside in a nursing home or long-term care facility at the time of diagnosis?   | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| 3. Did the patient receive intravenous antibiotic therapy, intravenous chemotherapy, wound care or attend a hemodialysis clinic within 30 days of diagnosis? | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| 4. Did the patient have a documented pulmonary infiltrate on chest radiograph or other chest imaging?  | <input type="checkbox"/> Yes | <input type="checkbox"/> No |

**(IF YOU ANSWERED YES TO QUESTION 1, 2, OR 3, OR NO TO QUESTION 4, THE PATIENT DOES NOT MEET CRITERIA FOR COMMUNITY-ACQUIRED PNEUMONIA AND SHOULD BE EXCLUDED)**

### Diagnostics

- |  |                              |                             |
|--|------------------------------|-----------------------------|
| 5. Was the patient admitted to an ICU due to complications of CAP?<br>(If No please skip to question 6)            | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| A. If Yes, were blood cultures sent?   | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| B. If Yes, was a sputum and/or endotracheal aspirate sent for Gram stain and culture?                              | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| C. If Yes, were cultures sent before antibiotics were administered?  | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| D. If Yes, were urinary antigen tests sent for <i>Legionella pneumophila</i> and <i>Streptococcus pneumoniae</i> ? | <input type="checkbox"/> Yes | <input type="checkbox"/> No |



**Therapeutics**

6. Were initial antibiotics consistent with institutional/national guidelines?  Yes  No

**72-hour Reassessment**

7. Was an organism isolated by culture within 72 hours of the first dose of antibiotics?  Yes  No

8. If an organism was isolated by culture, was it susceptible to the prescribed antibiotic?  
**(PRINT ANTIBIOTIC SUSCEPTIBILITY REPORT)**  Yes  No

9. Were antibiotics changed after culture results were available?  Yes  No  
If **YES**, please document antibiotic change:

\_\_\_\_\_

10. Was the patient initially prescribed an intravenous (IV) antibiotic with good oral bioavailability? (See Appendix Q1.A)  Yes  No

A. If **YES**, was the antibiotic changed to an oral formulation (PO), or was the patient started on a different oral antibiotic within 24 hours of being eligible for oral medications? (See Appendix Q1.B for criteria)  Yes  No

11. Total planned duration of antibiotics? \_\_\_\_\_ Days

## **Appendix A:**

Amoxicillin  
Amoxicillin/Clavulanate  
Azithromycin  
Cefpodoxime  
Ciprofloxacin  
Clindamycin  
Doxycycline  
Levofloxacin  
Linezolid  
Moxifloxacin  
Trimethoprim/Sulfamethoxazole

## **Appendix B:**

1. Patients must meet the following criteria:
  - A. Receiving oral or gastric tube intake.
  - B. Taking other oral medications.
  
2. Patients are considered inappropriate for IV to PO conversion if any of the following are present:
  - A. Mucositis.
  - B. Malabsorption syndrome or gastrointestinal motility disorder.
  - C. Severe nausea, vomiting or diarrhea.
  - D. Continuous nasogastric suctioning.
  - E. Continuous enteral feeds are contraindicated with oral ciprofloxacin, levofloxacin or moxifloxacin.

## Appendix Q2: CAP Assessment Score Card

Review admissions with a principal diagnosis of pneumonia using the CDC CAP Assessment form.

Patients meeting criteria for healthcare-associated pneumonia (Q1-Q3) should be categorized as CAP with risk factors for drug-resistant pathogens and excluded (track total excluded).

Patients without an infiltrate (Q4) but who still received >5 days of antibiotics for pneumonia should be excluded but noted as an area for improved stewardship education.

Summarize findings below.

	Number of patients	%	Appropriate management	% Appropriate
CAP with risk factors for drug-resistant pathogens			N/A	N/A
No infiltrate			N/A	N/A
<b>Management of Community-Acquired pneumonia</b>				
<b>ICU Admission</b>				
Blood cultures sent			Yes	
Respiratory culture sent			Yes	
Cultures prior to abx			Yes	
Urine antigens sent			Yes	
<b>All patients</b>				
Guideline-concordant initial abx			Yes	
Organism isolated at 72 hours			Yes	
Organism covered by initial abx			Yes	
Antibiotics modified for culture			Yes	
Initial IV abx with good oral bioavailability			N/A	
Candidate for PO but given IV			No	
Total IV duration			3–5 days	
Total PO duration (including Discharge)			5–7 days	

## Appendix R: Criteria for Appropriate (Empiric) Use of Vancomycin – IDSA Guidelines (Adults)

Clinical Syndrome	Comments
Vertebral osteomyelitis <sup>1</sup>	<i>Staphylococcus aureus</i> is most common cause
Cardiac device infections <sup>2</sup>	<i>Staphylococcus aureus</i> extremely common
Suspected bacterial meningitis <sup>3</sup>	To cover for penicillin-resistant <i>S. pneumoniae</i>
Severe sepsis/septic shock <sup>4</sup>	MRSA is a frequent cause of sepsis
CAP with concern for MRSA <sup>5</sup>	Linezolid is better for inhibiting toxin production. Look for lung abscess, cavitory infiltrates without aspiration.  Risk factors: ESRD, IVU, preceding flu, prior antibiotic therapy (FQ), critically ill/severe CAP
HCAP/VAP/HAP <sup>6</sup>	Late onset $\geq 5$ days OR risk factors for multi-drug-resistant (MDR) pathogens
Diabetic foot infections w/risk for MRSA <sup>7</sup>	Overall prevalence of MRSA in DFI is 5-30%.  MRSA coverage needed for mild/moderate infections (PEDIS 2/3) if there is a high risk of MRSA OR if the infection is clinically severe (PEDIS 4 = Local infection + 2 SIRS criteria).  Risk factors: Patient has a personal h/o MRSA infection or colonization within the past year; local prevalence of MRSA vs. MSSA is high (30% for moderate/severe, and 50% for mild infections)
Skin and soft tissue infection <sup>8</sup>	Purulent: severe SSTI (abscess) - patients who have failed incision and drainage plus oral antibiotics or those with SIRS (T $>38^{\circ}\text{C}$ , P $>90$ , RR $>24$ WBC $<12\ 000$ or $<400$ cells/ $\mu\text{L}$ ), or immunocompromised patients.  Non-purulent SSTI: Associated with penetrating trauma; MRSA infection at other body sites; nasal colonization with MRSA; IVU; Severe infection - patients who have failed oral antibiotic treatment or those with SIRS, immunocompromised, clinical signs of deeper infection such as bullae, skin sloughing, hypotension, or evidence of organ dysfunction; Necrotizing fasciitis, gas gangrene; Pyomyositis; Neutropenic fever with SSTI; Severe SSI $>4$ days after OR in penicillin-allergic patients
CLABS <sup>9</sup>	Empiric therapy for patients with indwelling lines and fever, until blood cultures result
Neutropenic fever <sup>10</sup>	For hospitalized patients with suspected catheter-related infection, skin infection, pneumonia, or hemodynamic instability. Also patients with IgE-mediated reactions to penicillins. May be stopped after 2 days if cultures negative.

Selected 1995 CDC/HICPAC Criteria relevant to hospitalists,<sup>11</sup> studied in Kumana et al, 2001.<sup>12</sup>

Appropriate Use	Inappropriate Use
Treatment of infections with beta-lactam resistant gram-positives	Empiric therapy for neutropenic fever, unless inflamed vascular catheter (recent guidelines add hypotension, SSTI, and pneumonia)
Treatment of gram-positives in patients with serious allergies to beta-lactams	Treatment of a single positive blood culture for Coag-negative staph (contamination likely)
	Continued empiric use for presumed infections in patients whose cultures are negative for beta-lactam resistant gram-positives, attempted eradication of MRSA colonization. Treatment of beta-lactam sensitive organisms in dialysis patients (chosen for dosing convenience)

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## Appendix S1: Surveillance Form Appropriate Use of Vancomycin - CDC

### Assessment of Appropriateness of Antibiotic Use for Resistant Gram-Positive Infections

A. Date: \_\_\_\_\_ Gender: Male Female  
Age: \_\_\_\_\_ Service: \_\_\_\_\_

B. Please indicate if daptomycin, linezolid or vancomycin was used for any of the following indications:

1. Single blood culture positive for coagulase-negative staphylococci, *Bacillus* species, *Corynebacterium* species and/or diphtheroids in the absence of prosthetic joints, prosthetic cardiac valves, or cardiac implantable electronic devices (including AICD, LVAD and pacemaker). \_\_\_\_\_ Yes \_\_\_\_\_ No

2. Documented infection with Streptococci, Enterococci, or Staphylococci susceptible to a  $\beta$ -lactam antibiotic, in a patient without documented allergy to  $\beta$ -lactam antibiotics. (If allergy to  $\beta$ -lactam, please answer questions in section C) \_\_\_\_\_ Yes \_\_\_\_\_ No

3. Continued empiric use after 72h despite no cultures collected or negative cultures. (Exceptions should be made for neutropenic patients with an ANC <500 cells/ $\mu$ L and patients transferred from outside facilities) \_\_\_\_\_ Yes \_\_\_\_\_ No

A. If Yes, was an indication documented? (Please specify indication below) \_\_\_\_\_ Yes \_\_\_\_\_ No

\_\_\_\_\_

B. If Yes, were cultures collected? \_\_\_\_\_ Yes \_\_\_\_\_ No

C. If cultures were collected, were antibiotics administered before collection? \_\_\_\_\_ Yes \_\_\_\_\_ No

4. Treatment of methicillin-resistant *Staphylococcus aureus* (MRSA) isolated from cultures of the nares or stool (represent colonization). \_\_\_\_\_ Yes \_\_\_\_\_ No

C. IF ALLERGY REPORTED TO  $\beta$ -LACTAM ANTIBIOTIC, PLEASE ANSWER THE FOLLOWING:

1. Drug name \_\_\_\_\_

2. Was allergy/adverse drug reaction documented? \_\_\_\_\_ Yes \_\_\_\_\_ No

3. Documented allergy or adverse drug reaction \_\_\_\_\_

## Appendix S2: Vancomycin Scoring Assessment: Appropriateness of Vancomycin Use for Gram-Positive Infections

Use the CDC Tool [Assessment of Appropriateness of Antibiotic Use for Resistant Gram-Positive Infections] to review the charts of 50 patients on the hospitalist service who received vancomycin for >72 hours in a designated time period.

Metric	Number of patients	Appropriate management	% Appropriate
Indications for vancomycin use			
Treatment of likely contaminant (Q1)		NO	
Treatment of beta-lactam sensitive bacteria, no allergy documented (Q2)		NO	
Prolonged empiric use (Q3)		NO	
Treatment of MRSA colonization		NO	
Best practices			
Cultures prior to antibiotics		YES	
Clear documentation of drug allergy		YES	



## Appendix T: Tool for Performing Institutional Assessment

### TASK Perform an institutional assessment of your current practice

Task 1 Administrative support assignment \_\_\_\_\_

Time line for completing \_\_\_\_\_

Task 2 Multidisciplinary team assignment \_\_\_\_\_

Time line for completing \_\_\_\_\_

Task 3 Data flow/metrics assignment \_\_\_\_\_

Time line for completing \_\_\_\_\_

Task 4 Understanding current discharge process and propose areas for standardization assignment  
\_\_\_\_\_

Time line for completing \_\_\_\_\_

Task 5 Family/caregiver preparedness assignment \_\_\_\_\_

Time line for completing \_\_\_\_\_

Task 6 Medication safety issues assignment \_\_\_\_\_

Time line for completing \_\_\_\_\_

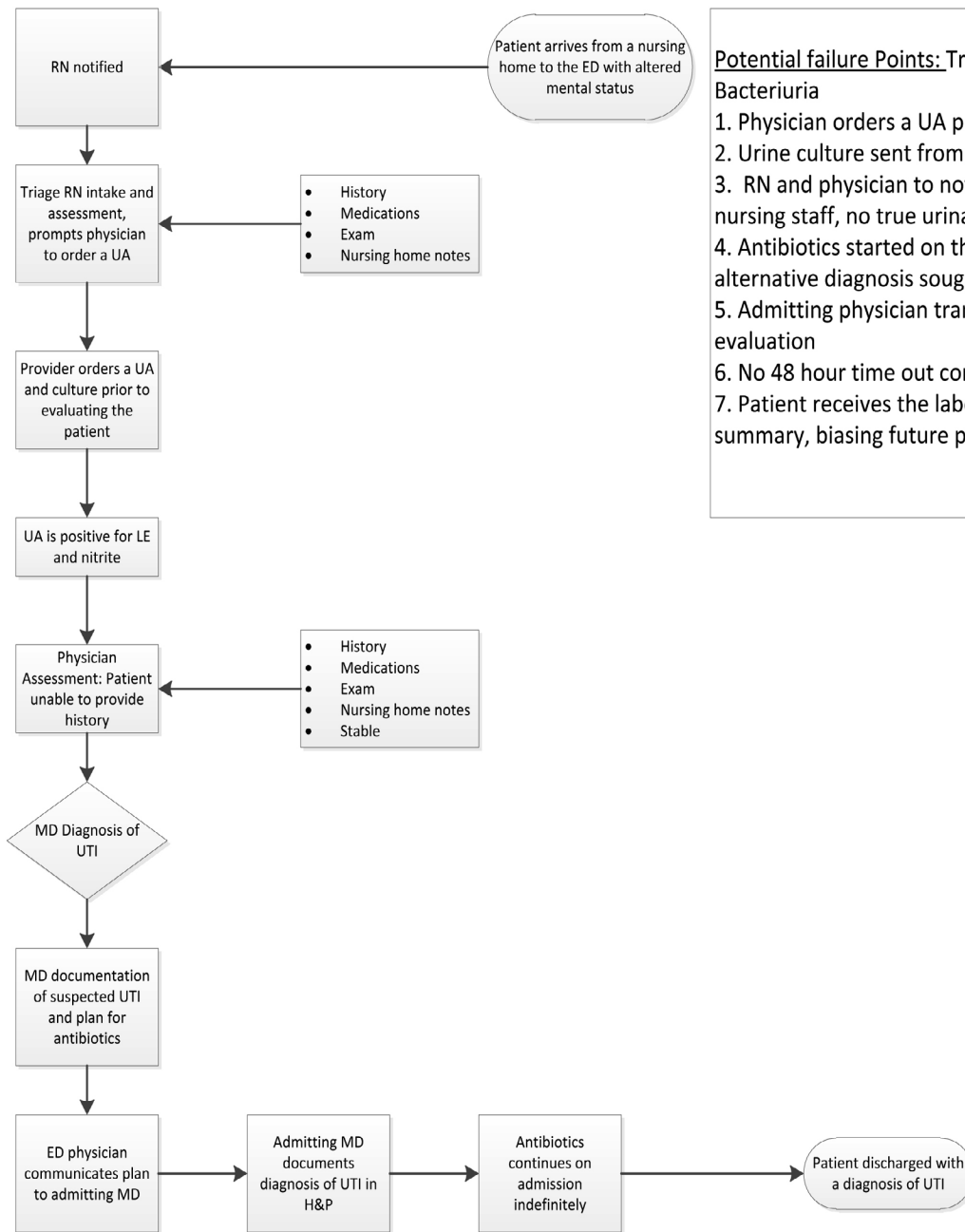
Task 7 Follow-up care assignment \_\_\_\_\_

Time line for completing \_\_\_\_\_

Task 8 Educational issues assignment \_\_\_\_\_

Time line for completing \_\_\_\_\_

Figure 1. Process Flow Map



**Potential failure Points: Treatment of Asymptomatic Bacteriuria**

1. Physician orders a UA prior to patient history
2. Urine culture sent from old catheter
3. RN and physician to not obtain history from family or nursing staff, no true urinary symptoms elicited
4. Antibiotics started on the basis of a positive UA, no alternative diagnosis sought
5. Admitting physician transmits ED diagnosis without re-evaluation
6. No 48 hour time out conducted to re-evaluate antibiotics
7. Patient receives the label of "recurrent UTIs" in discharge summary, biasing future providers

## Appendix U: Pharmacy Daily Rounding List

[<https://www.shea-online.org/Portals/0/PDFs/Intermountain-Antimicrobial-Stewardship-Checklist.pdf>]

### Antimicrobial Stewardship Checklist

Print a list of patients on antibiotics for your coverage area. Review each prescribed antibiotic for the following.

#### Antibiotic Indication

- Review for ***Antimicrobial Indication*** and concordance with the ***Antimicrobial Prescribing Procedure***

#### Antibiotic Restrictions

- Determine if antimicrobial is a ***Restricted Antimicrobial*** and follow up on pending approvals

#### Microbiology

- Review microbiology to evaluate for ***Bug-Dug Mismatch***
- For patients with positive clinical cultures only!** Review all patients on vancomycin, imipenem, meropenem, piperacillin-tazobactam, and/or cefepime per the ***De-escalation*** protocol
- Determine if there is duplicate or missing treatment of ***Anaerobes***
- Determine if the syndrome present meets criteria for ***When to Consult Infectious Diseases***

#### Dose, Route, and Administration

- Review antimicrobial **dose and frequency** based on indication, patient weight, and patient renal function; refer to ***Antimicrobial Dosing Guidelines*** for assistance.
- Review antimicrobial **route** to determine if ***IV to PO Conversion*** should be recommended.
- Review antimicrobial for **duration**.

\*More detail about ***these procedures*** is available on the Antimicrobial Stewardship website.

## Appendix V: Summary of Evidence for Shorter Durations of Antibiotics

A majority of these studies are excerpted from Table 2 of Barlam et al, CID 2016<sup>1</sup> “Meta-analyses and Examples of Randomized Clinical Studies Comparing Shorter versus Longer Duration of Antibiotics.” (Adults only, community-acquired patients)

Reference	Clinical Condition/ Population	Sample size	Treatment duration, d	Drugs	Clinical Outcomes Measures	Findings
<b>Meta-analyses</b>						
Dimopoulos et al, 2008 <sup>2</sup>	CAP: Adults and children	1,303	3–7 vs 5–10	Multiple regimens	Clinical success, relapse, mortality, adverse events	No significant differences between groups
Milo et al, 2005	UTI: Uncomplicated cystitis in women	9,605	3 vs 5–7	Multiple regimens	Clinical success and bacteriologic cure	No difference in clinical cure, but 3 d increased bacteriologic failure
El Moussaoui et al, 2008 <sup>3</sup>	AECB: Adults with mild-moderate COPD exacerbations	10,698	≤5 vs >5	Multiple regimens	Clinical success, bacteriologic cure	No significant difference between groups
Pugh et al, 2015 <sup>4</sup>	HAP: Critically ill adults	598–733	7–8 vs 10–15	Multiple regimens	Mortality, recurrence	Decreased antibiotic use and subsequent resistant organism, no increase in mortality or recurrence (except with NF-GNB)
<b>Randomized Controlled Trials</b>						
Talan et al, 2000 <sup>5</sup>	UTI: Women with acute uncomplicated pyelonephritis (outpatient)	214	7 vs 14	Ciprofloxacin vs TMP/SMX	Bacteriologic and clinical cure	Shorter course associated with a higher bacteriologic cure rate (99% vs 89%, p=0.004) and clinical cure rates (96% vs 83%, p=0.002)
Singh et al, 2000	“VAP”: Adults in ICU with infiltrates and CPIS ≤6	81	3 vs 10-21	Ciprofloxacin vs multiple	Mortality, length of ICU stay, superinfections	No significant difference in mortality or LOS. Fewer superinfections in short course group

Hepburn et al, 2004 <sup>6</sup>	SSTI: Adults with uncomplicated cellulitis	87	5 vs 10	Levofloxacin	Clinical success	No significant differences between groups
Prokocimer et al, 2013	SSTI: Adults with cellulitis, abscess, wound infection	668	6 vs 10	Tedizolid v linezolid	Clinical success	No significant difference between groups
El Moussaoui et al, 2006 <sup>7</sup>	CAP: Adults with mild-moderate CAP (PSA $\leq$ 110)	119	3 vs 5	Amoxicillin	Clinical and radiological success	No significant differences between groups
File et al, 2007 <sup>8</sup>	CAP: Adults mainly with mild-moderate CAP	510	5 vs 7	Gemifloxacin	Clinical and microbiological success	No significant differences between groups
Sandberg et al, 2012	UTI: Women with acute uncomplicated pyelonephritis	248	7 vs 14	Ciprofloxacin	Clinical success, recurrence	No significant differences between groups

CAP: community-acquired pneumonia; UTI: urinary tract infection; AECB: Acute exacerbation of chronic bronchitis; NF-GNB: non-fermenting gram-negative bacilli; HAP: hospital-acquired pneumonia; VAP: ventilator-acquired pneumonia; HCAP: healthcare-associated pneumonia; SSTI: skin and soft tissues infections

## References

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## Appendix W: Plan, Do, Study, Act Cycle

[<http://www.ihl.org/resources/Pages/Tools/PlanDoStudyActWorksheet.aspx>]

### PDSA Worksheet for Testing Change

**Aim:** (overall goal you wish to achieve)

*Every goal will require multiple smaller tests of change*

Describe your first (or next) test of change:	Person responsible	When to be done	Where to be done

Plan

List the tasks needed to set up this test of change	Person responsible	When to be done	Where to be done

Predict what will happen when the test is carried out	Measures to determine if prediction succeeds

**Do** Describe what actually happened when you ran the test

**Study** Describe the measured results and how they compared to the predictions

**Act** Describe what modifications to the plan will be made for the next cycle from what you learned

## Appendix X: Digital Resources - Clinical Decision Support for Treatment of Common Infections

### General Stewardship Resources:

- CDC Get Smart for Healthcare – a comprehensive website for stewardship implementation. Very little in terms of guidelines for treatment of specific inpatient infections on the CDC stewardship page. Outpatient treatment recommendations are here for cystitis, bronchitis, and pharyngitis: <http://www.cdc.gov/getsmart/community/for-hcp/outpatient-hcp/adult-treatment-rec.html>.
- Outpatient management of SSTI in the era of MRSA: <http://www.cdc.gov/mrsa/pdf/Flowchart-k.pdf>
- Guideline Central (free to SHEA members, \$5.95 digital, \$7.95- \$11.95 per pocket card), SHEA/ IDSA Guidelines in glossy algorithm format – limited library (C diff, infection prevention, CAP, SSTI, cIAB, DFI, MRSA, influenza). (<https://www.guidelinecentral.com/shop/specialty/infectious-disease>)

### Mobile apps:

- AgileMD – (“FREE”) an online and mobile library where multiple institutions deposit their clinical pathways, calculators, monographs. University of Nebraska Antimicrobial Stewardship has uploaded some excellent guidelines for most common infections (text blocks mostly). Multiple price points depending on level of complexity – free to download the app. Many institutions charge for access to their content (\$19.99). Always growing. Also offers institutional subscriptions for up to \$75,000 for clinical decision support integrated into your EMR, or curated for your staff. (<https://www.agilemd.com/home>)
- Johns Hopkins Guides: ABX (\$29.95/year) – frequently updated evidence based app with extensive information on the treatment of most commonly encountered infectious diseases. Text only. (<http://www.hopkinsguides.com/hopkins/ub>)
- Sanford Guide app (\$29.99/year) – updated monthly. The classic antibiotic guide, recommendations by pathogen and syndrome. Also has a Lab Diagnosis module to guide utilization and interpretation of cultures (IDSA 2013). (<http://www.sanfordguide.com/>)
- UCLA Antibiotic Guide – (Free app!) Extensive online resources, clinical pathways for main common infections – SSTI, CAP, abdominal infections, UTI/CAUTI, CLBSI (text only, no flowcharts), pdf downloadable in sections.

### Software builders:

- Dorsata – an online and mobile platform for building and disseminating clinical guidelines and pathways in a user friendly app form, similar to Microsoft Visio. Used by a number of large stewardship programs. Collaborative development. Yearly subscription costs of \$2,100-\$20,000+ depending on complexity of content. (<https://www.dorsata.com>)
- Applied Pathways – (Contract pricing) a tech startup company that helps hospitals write and disseminate clinical pathways using their Curion platform. Also can be integrated into the EMR. Has telemedicine platform as well. (<http://appliedpathways.com/>)
- AgileMD (see above)



**Institutional antibiotic guidelines (mainly PDFs):**

- Cleveland Clinic Antimicrobial Guidelines – Clean, easy to read, comprehensive. Searchable, downloadable, and indexed PDF. Includes microbiology data, mechanisms of antibiotics, nice summary tables for different infections (treatment durations are a little long for most infections, however). Warfarin interaction table, antibiotics in pregnancy/lactation tables, which are helpful. Adult vaccination schedules. Not referenced, not updated since 2013.  
(<http://www.clevelandclinicmeded.com/medicalpubs/antimicrobial-guidelines/>)
- Columbia University Medical Center Stewardship Program – Numerous clinical references including detailed algorithms for CAP with PORT score stratification, neutropenic fever, CLSI breakpoints table (2008)  
([http://www.cumc.columbia.edu/dept/id/clinical\\_references.html](http://www.cumc.columbia.edu/dept/id/clinical_references.html))
- Jackson Memorial (U of Miami) Stewardship Program – Extensive stewardship website with multiple helpful protocols, IV to PO conversation, ID algorithms (Gram stains, CAUTI, CAP, DFI, UTI in women, mostly from 2008)  
(<http://ugotabug.med.miami.edu/jmh-antimicrobial-stewardship-program/>)
- Johns Hopkins Antibiotic Guidelines – (FREE) Institution-specific recommendations published by the Johns Hopkins Hospital Antimicrobial Stewardship team. Online as a searchable, downloadable pdf. Includes drug monographs and recommendations by infectious syndrome.  
([http://www.hopkinsmedicine.org/amp/guidelines/Antibiotic\\_guidelines.pdf](http://www.hopkinsmedicine.org/amp/guidelines/Antibiotic_guidelines.pdf))
- Nebraska Medicine Stewardship Program – Very nice website with short educational videos. Antibiotic guidelines are on AgileMD for free. Unique content includes procalcitonin guidance, table on “pathogen vs. contaminant,” video on micro lab MIC interpretation, HCAP/VAP guideline, video on stewardship in long term care facilities, table for recommended treatment based on rapid diagnostics. Updated 2012.  
(<http://www.nebraskamed.com/careers/education-programs/asp/plans>)
- Wake Forest Antimicrobial Stewardship Program – Nice user friendly website with limited but concise guidelines/pathways with algorithms, downloadable PDF sections. CAP, HCAP, sepsis, procalcitonin, neutropenic fever, C diff. Single pager on empiric therapy in the ED for non-septic patients. Also contains an Antibiotic Stewardship Curriculum for medical students (online ppt). (<http://www.wakehealth.edu/School/CAUSE/>)

**Other stewardship program websites:**

- Ohio State University Stewardship Program – (Requires a login for most content). Free content includes organism flow charts, common micro gram stain interpretations, antibiotic PK/PD summary. (<http://rx.osumc.edu/asp2/index.html>)
- Stanford Medicine Stewardship Program – limited clinical pathways, mainly empiric antibiotics for sepsis based on source, and treatment of refractory C diff. (<http://med.stanford.edu/bugsanddrugs/guidebook.html>)
- Barnes-Jewish Toolbook (Dorsata) – (free login upon request, maybe) – Barnes Jewish Institutional Antibiotic guidelines. Drug monographs, limited clinical pathways. (<http://bjhtoolbook.wustl.edu/contact.html>)
- University of Kentucky Stewardship Program – free online PDF sections, limited clinical pathways for meningitis, antifungals, IAB, and neutropenic fever, nice VAP protocol document. Referenced.  
(<http://www.hosp.uky.edu/pharmacy/amt/default.html>)
- University of Wisconsin Stewardship Website – Primarily a list of articles pertaining to different stewardship topics. (<http://www.uwhealth.org/antimicrobial-stewardship/main/36408>)

## Appendix Y: Sample EPIC Order Sets for Common Infections

(Developed by the Johns Hopkins Medicine Antibiotic Stewardship Team, adapted from the Antibiotic Guidelines 2014-2015)

Order Sets		? Actions
<b>GENERAL ADULT PNEUMONIA FOCUSED</b>		
<b>General</b>		
<input checked="" type="checkbox"/> Incentive Spirometry	Routine, Every hour while awake First occurrence Today at 1507 Until Specified	
<b>Labs</b>		
<b>Pathogen-Specific Labs</b>		
<input type="checkbox"/> Bacterial Culture/Smear, Respiratory	Once, Sputum, expectorated	
<input type="checkbox"/> Legionella Antigen, Urine	Once	
<input type="checkbox"/> Strep Pneumo Urinary Antigen	Once	
<b>Respiratory Virus Testing</b>		
Respiratory virus testing is recommended during respiratory virus season and at other times on a case-by-case basis. The complex respiratory panel should be ordered for patients with the following: ICU admission, structural lung disease (e.g. cystic fibrosis, bronchiectasis) and/or immunocompromise (e.g., solid organ transplant, hematologic malignancy, BMT, active chemotherapy, HIV, use of immunosuppressive drugs including glucocorticoids).		
<input type="checkbox"/> Respiratory Virus Panel-Standard	Once, Nasopharyngeal Swab	
<input type="checkbox"/> JHM RESP VIRUS PANELS COMPLEX		
<b>Blood Cultures</b>	0 of 2 selected	
<b>Medications</b>		
<b>Respiratory</b>	0 of 1 selected	
<b>Mucolytic/Antitussive</b>	0 of 2 selected	
<b>Community-acquired pneumonia (CAP), Empiric Antibiotics</b>		
<b>MRSA Pneumonia:</b> The vast majority of patients with CAP do not need vancomycin. Consider vancomycin in patients with CXR findings suggestive of MRSA pneumonia including necrotizing pneumonia with cavitation, dense multilobar consolidation, or patients who are critically ill in the ICU.		
NOTE: If patient is coming from a nursing home or long-term care facility, see Healthcare-acquired pneumonia.		
<b>CAP</b>		
Recommendations are for a beta-lactam (ceftriaxone or amp/sulbactam) + azithromycin. If the patient has received macrolides or fluoroquinolones prior to admission, then no azithromycin is needed. See "CAP" section in the Antibiotic Guidelines. Oral therapy is preferred for azithromycin and moxifloxacin since 100% bioavailable. If the patient has a severe PCN allergy, then use moxifloxacin alone.		
For obese patients (>100 kg), consider higher doses of antibiotics.		
<b>Antibiotic Guidelines</b>		
<input type="checkbox"/> cefTRIAxone (ROCEPHIN) IV	1 g, Intravenous, Every 24 hours	
<input type="checkbox"/> ampicillin-sulbactam (UNASYN) IVPB		
<input type="checkbox"/> azithromycin (ZITHROMAX) tablet	500 mg, Oral, Daily, for 3 days	
<input type="checkbox"/> azithromycin (ZITHROMAX) IVPB	500 mg, Intravenous, Every 24 hours, for 3 days	
<input type="checkbox"/> moxifloxacin (AVELOX) tablet - Severe PCN allergy	400 mg, Oral, Daily	

#### Healthcare-acquired pneumonia (HCAP), Empiric Antibiotics

##### HCAP - Mild/Moderate (Not requiring ICU/IMC, no or minimal hypoxemia, no hypotension)

Consider adding azithromycin if patient is immunocompromised (organ transplant, hematologic malignancy, BMT, active chemotherapy, immunosuppressive drugs/glucocorticoids) or coming from a nursing home or long term care facility (to cover Legionella).

Recommendations are for ceftriaxone OR moxifloxacin alone for severe PCN allergy. See below for MDR risk factors.

Patient with history of or strong risk factors for Pseudomonas and other resistant Gram-negative organisms (e.g., bronchiectasis; broad-spectrum antibiotics for > 7 days in the past month; prolonged hospitalization > 7 days; recent mechanical ventilation > 48 hours; immunocompromised due to solid organ transplant, hematologic malignancy, BMT, active chemotherapy, prednisone >= 20 mg daily for >= 3 weeks): use HCAP-Severe instead.

For obese patients (>100 kg), consider higher doses of antibiotics.

##### Antibiotic Guidelines

- cefTRIAXone (ROCEPHIN) IV  
1 g, Intravenous, Every 24 hours
- azithromycin (ZITHROMAX) tablet  
500 mg, Oral, Daily, for 3 days
- azithromycin (ZITHROMAX) IVPB  
500 mg, Intravenous, Every 24 hours, for 3 days
- moxifloxacin (AVELOX) tablet - Severe PCN allergy  
400 mg, Oral, Daily
- moxifloxacin (AVELOX) IVPB - Severe PCN allergy  
400 mg, Intravenous, Every 24 hours

##### HCAP - Severe (Hypoxemia, multilobar consolidation, severe sepsis, or requiring ICU)

Choose cefepime or piperacillin-tazobactam +/- vancomycin.

Consider adding azithromycin if patient is immunocompromised (organ transplant, hematologic malignancy, BMT, active chemotherapy, immunosuppressive drugs/glucocorticoids) or coming from a nursing home or long term care facility (to cover Legionella).

For severe penicillin allergy, page Antibiotic Approval.

##### Antibiotic Guidelines

- cefepime (MAXIPIME) IVPB
- piperacillin-tazobactam (ZOSYN) IVPB
- azithromycin (ZITHROMAX) tablet  
500 mg, Oral, Daily, for 3 days
- azithromycin (ZITHROMAX) IVPB  
500 mg, Intravenous, Every 24 hours, for 3 days
- Vancomycin - Peripheral Line

**Order Sets** ? Actions

▼ **JHH-BMC Adult Cellulitis Focused Manage My Version** Add Order

**Cellulitis:** Contains general orders common to most admissions and orders specific to cellulitis treatment.

If concerned for rapidly progressive or necrotizing infection of deep soft tissue or post-operative wound, please consider adding gram negative coverage and clindamycin for toxin inhibition. Calculate a LRINEC score to predict risk of necrotizing fasciitis. See Johns Hopkins Antibiotic Guidelines section on skin and soft tissue infections for antibiotic recommendations.

Antibiotic Guidelines  
LRINEC Score Calculator

▼ **General**

▼ **Nursing Interventions**

- Elevate Extremity Routine, Until discontinued starting Today at 1519 Until Specified  
Elevate affected extremity to level above patient's heart.
- Mark area of Skin Routine, Until discontinued starting Today at 1519 Until Specified  
Mark area of erythema with skin pen Now and then PRN.

▼ **Labs**

▼ **Wound Cultures**

**Cultures of intact skin and open wounds are not acceptable.**  
For abscesses and draining wounds, aspirates for Gram-stain and culture are preferable to swabs. Anaerobic cultures are rarely needed and require aspirate specimens in special media.

- Bacterial Culture/Smear, Aerobic, Misc Once, DO NOT send cultures of chronic wounds.

▶ **Blood Cultures** 0 of 2 selected

▼ **Nonpurulent Cellulitis (intact skin, no purulent drainage)**

Most frequently due to beta-hemolytic streptococci and MSSA.

For obese patients (>100 kg), consider higher doses of antibiotics.

Antibiotic Guidelines

▼ **Antibiotics - Mild Cellulitis**

- amoxicillin-clavulanate (AUGMENTIN) tablet
- cephalexin (KEFLEX) capsule
- clindamycin (CLEOCIN) capsule - PCN allergy 300 mg, Oral, Every 8 hours scheduled

▼ **Antibiotics - Moderate/Severe Cellulitis**

- ceFAZolin (ANCEF) IV
- ampicillin-sulbactam (UNASYN) IVPB
- clindamycin (CLEOCIN) IV - PCN allergy 600 mg, Intravenous, Every 8 hours scheduled

▼ **Purulent Cellulitis (with purulence or a drainable abscess)**

Purulence usually indicates MSSA or MRSA. Abscesses should be drained.  
Note: If abscess is completely drained, diameter of abscess/cellulitis less than 5 cm, patient has no evidence of sepsis and is immunocompetent/non-diabetic, no antibiotics are needed.

For obese patients (>100 kg), consider higher doses of antibiotics.

Antibiotic Guidelines

▼ **Antibiotics - Mild Cellulitis**

- sulfamethoxazole-trimethoprim (BACTRIM DS) 800-160 mg per tablet
- doxycycline hyclate (VIBRAMYCIN) capsule 100 mg, Oral, 2 times daily
- clindamycin (CLEOCIN) capsule 300 mg, Oral, Every 8 hours scheduled
- clindamycin (CLEOCIN) IV - Need for parenteral therapy 600 mg, Intravenous, Every 8 hours scheduled

▼ **Antibiotics - Moderate/Severe Cellulitis - JHH**

If the patient has moderate or severe disease and has a severe vancomycin allergy, please contact ID via the approval pager to discuss alternatives.

- Vancomycin - Peripheral Line

▼ **Antibiotics - Moderate/Severe Cellulitis - BMC**

If the patient has moderate or severe disease and has a severe vancomycin allergy, please contact ID via the approval pager to discuss alternatives.

- Vancomycin - Peripheral Line

## CAUTI and Nephrostomy Tubes (see Antibiotic Guidelines)

## Medications

0 of 5 selected

## Acute Cystitis Oral Medication

## Acute Cystitis IV Medication

The Antimicrobial Stewardship and DOM HVCC recommends **against** treating asymptomatic bacteriuria/pyuria. Cystitis symptoms include frequency; urgency; dysuria; suprapubic pain.

For **complicated** infections (e.g., associated with stones, urologic abnormalities, obstruction, pregnancy) extend recommended duration to 7-14 days.

Oral therapy is preferred for cystitis and should be given unless the patient is unable to take oral therapy.

- cefazolin (ANCEF)

## Acute Pyelonephritis Medication

Acute pyelonephritis is defined as signs and symptoms of an ascending UTI (e.g., fever, flank pain) together with pyuria and bacteriuria. Most patients have other evidence of upper tract disease such as leukocytosis, WBC casts or abnormalities on imaging.

Oral therapy should be used if the organism is susceptible (see Antibiotic Guideline for recommendations). Duration of therapy should include initial empiric IV therapy.

If onset occurs after hospitalized >48 hours, use urosepsis orders below.

- ceftRIAXone (ROCEPHIN)  
1 g, Intravenous, Every 24 hours, for 7 days
- ertapenem (INVANZ)

## Acute Pyelonephritis if Severe PCN Allergy

Acute pyelonephritis is defined as signs and symptoms of an ascending UTI (e.g., fever, flank pain) together with pyuria and bacteriuria. Most patients have other evidence of upper tract disease such as leukocytosis, WBC casts or abnormalities on imaging.

Severe PCN allergy is defined as anaphylaxis, Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis, or Drug Reaction with Eosinophilia and Systemic Symptoms.

Oral therapy should be used if the organism is susceptible to an appropriate antibiotic (see Antibiotic Guideline for recommendations). Total duration of therapy should include initial empiric IV Therapy.

If onset occurs after hospitalized >48 hours, use urosepsis orders below.

**Choose** aztreonam OR gentamicin.

- aztreonam (AZACTAM)
- gentamicin (GARAMYCIN)

## Urosepsis Medication

Urosepsis is defined as SIRS/sepsis with a urinary source of infection.

- cefepime (MAXIPIME)

## Urosepsis Medication if Severe PCN Allergy

Urosepsis is defined as SIRS/sepsis with a urinary source of infection

Severe PCN allergy is defined as anaphylaxis, Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis, or Drug Reaction with Eosinophilia and Systemic Symptoms.

Choose **BOTH** agents if patient has had extensive antibiotic exposure or is severely ill.

- aztreonam (AZACTAM)
- gentamicin (GARAMYCIN)

## Appendix Z: Use of Procalcitonin for Antibiotic Stewardship

### Background

#### Biology of Procalcitonin

Procalcitonin (PCT), the precursor to calcitonin, is a peptide that is up-regulated in numerous tissues throughout the body in response to bacterial stimuli (lipopolysaccharide, TNF $\alpha$ ) but not by viral infections<sup>1-4</sup> thus serving as a helpful tool in guiding antibiotic use. PCT levels increase within 4 to 6 hours of initiation of bacterial infection or intravenous endotoxin, while increases in CRP level and ESR require 24 or more hours.<sup>1,5,6</sup> The normal PCT level in an uninfected person based on highly sensitive assays is  $0.033 \pm 0.003$  ng/mL, i.e. 0.04 for the Kryptor PCT assay.<sup>7</sup>

#### Procalcitonin and Antibiotic Stewardship – the Evidence

To date, there have been 32 randomized controlled trials in adults comparing procalcitonin-guided antibiotic use to standard practice for either respiratory tract infections, critical care, or Emergency Department use (Table 1). Twenty-four of these trials have been systematically reviewed in 2 large series. Dr. Schuetz et al. conducted a Cochrane Review in 2012 of procalcitonin guided therapy in respiratory infections, reviewing 14 randomized trials.<sup>8</sup> Marie Westwood et al. conducted a systematic review and cost-effectiveness analysis for the UK in 2015 of procalcitonin-guided therapy for treatment of sepsis in the ICU and suspected bacterial infections in the emergency department.<sup>9</sup> The conclusions of both reviews finding that procalcitonin use in study protocols significantly reduces antibiotic use without increasing adverse events.

#### Procalcitonin in the USA

The U.S. Food and Drug Administration (FDA) has cleared for marketing through the 510(k) process the BRAHMS PCT sensitive KRYPTOR (Brahms USA, Inc., Annapolis, MD), the VIDAS BRAHMS PCT (bioMerieux, Inc., Hazelwood, MO), and the BRAHMS PCT LIA (BRAHMS Diagnostica, LLC, Tracys Landing, MD) quantitative assays to determine the concentration of PCT in serum and plasma. These devices utilize different technologies and instruments to obtain results but have a similar indication for use, which is to aid in the assessment of risk progression to severe sepsis and septic shock in critically ill patients on the first day of admission to ICU. The devices are intended to be used in conjunction with other laboratory findings and clinical assessments to determine whether an infection is bacterial or viral, thus, potentially avoiding unnecessary use of antibiotics. The FDA approved a second indication for PCT in 3/2016 as an aid in prediction of 28-day mortality in patients with severe sepsis and septic shock. The FDA has not yet approved PCT for use in respiratory infections. Aetna currently covers the use of PCT as medically necessary both for sepsis and in respiratory infections.

Branche et al. conducted the first all-USA procalcitonin study, an RCT in adults hospitalized with non-pneumonic LRTI in New York. Inclusion criteria were adults  $\geq 21$  years of age with symptoms compatible with LRTI but without a definitive pneumonia on chest x-ray (“ambiguous findings”). They excluded all of the high-risk patients (sepsis, ICU admissions, etc), in order to demonstrate safety and efficacy in the “low-hanging fruit” of respiratory tract infections.

They obtained 2 PCT levels and viral PCR testing at enrollment, and directed clinicians using the standard PCT algorithm recommended by Schuetz in his reviews: For PCT values of  $\leq 0.1$  ng/mL, initiation of antibiotic treatment is strongly discouraged; for values of 0.11–0.24 ng/mL, initiation is discouraged; for values of 0.25–0.49 ng/mL, initiation is encouraged; and for values of  $\geq 0.5$  ng/mL, initiation is strongly encouraged.” Results: Algorithm adherence was 64%. In low risk patients (**positive for virus and had a low PCT level**) there was a trend toward fewer days of antibiotics prescribed (median, 2 days [IQR, 1–6 days] vs 4 days [IQR, 0–8 days];  $P = .11$ ), **with significantly fewer patients discharged receiving antibiotics** (20% vs 45%;  $P = .002$ ). Among subjects for whom treating physicians adhered to the algorithm (64%) revealed a significantly shorter duration of therapy, compared with the duration among nonintervention subjects (median, 2 days [IQR, 0–3 days] vs 4 days [IQR, 0–8 days];  $P = .004$ ).

**Procalcitonin has been adopted for general use by multiple stewardship programs throughout the United States.** The University of Nebraska and Providence St. Vincent in Portland, Oregon both use the biomarker in daily practice and are currently analyzing the impact on antibiotic use. Dr. Gilbert and his group and Oregon have published a number of studies on their use of procalcitonin in practice.<sup>10-13</sup> These programs emphasize that **procalcitonin should not be used in isolation** but should be taken as an adjunct to traditional clinical assessment tools and be used in the context of an ongoing intervention champion.

## Procalcitonin in practice

Several uses for PCT have been demonstrated in practice:

Use	Comment	FDA Package Insert	References
Determining the risk of progression to septic shock on the first ICU day	PCT levels above 2.0 µg/L are associated with a higher risk of progression to severe sepsis and/or septic shock than PCT levels below 0.5 µg/L.	YES	Muller 2000 <sup>14</sup> and Harbarth 2001 <sup>15</sup>
Predicting cumulative 28-day likelihood of mortality in critically ill septic patients	A PCT level that declines ≤80% from the day that severe sepsis or septic shock was clinically diagnosed (Day 0, or Day 1) to Day 4 is associated with a higher cumulative 28-day risk of all-cause mortality than a decline >80%.	YES	Luyt 2005 <sup>16</sup> and Brunkhorst 1998 <sup>17</sup>
Determining whether empiric therapy is effective, or whether source control has been adequately achieved.	PCT levels should fall by ~50% per day (in persons with normal renal function) when the patient is on effective antibiotics and the source is controlled. <sup>18</sup> A cutoff of <0.1 ng/mL is a widely used cutoff for discontinuing antibiotics once started.	YES	Charles 2009 <sup>18</sup> ProHOSP Trial <sup>19</sup> PRORATA Trial <sup>4</sup>
Differentiating bacterial infections from non-bacterial infections and non-infectious conditions.	PCT levels >0.1-0.25 can indicate a bacterial infection depending on the clinical context	YES	Christ-Crain 2004 <sup>20</sup>
Guiding empiric antibiotic therapy in patients with acute exacerbations of chronic bronchitis, community-acquired pneumonia, and sepsis	In multiple trials, 2 low PCT levels in the first 4 to 6 hours of admission resulted in fewer patients started on empiric antimicrobials.	NO	See Table 1

Integration with microbiology results can be challenging, as the sensitivity and specificity of cultures and other assays are not perfect either. A suggested schema for interpretation with microbiology was developed by David Gilbert, MD and is useful in clinical practice (see Table 2).<sup>10</sup> The trials using serial procalcitonin measurements<sup>19,21</sup> have seen larger reductions in antibiotic use than those using single measurements. Investigators have used a variety of methods to encourage prescribers to use the algorithms, including initial education interventions to create buy-in, followed by distribution of pocket-cards, or website links.<sup>22</sup> Schuetz has recommended a three-tiered approach to the application of PCT in respiratory tract infections, using different cutoffs based on pre-test probability for bacterial infection and the acuity of illness.<sup>23</sup>

Numerous “non-infectious” conditions have been shown to cause elevations in PCT such as inhalational injury, pulmonary aspiration, severe burns, pancreatitis, heat stroke, mesenteric infarction, multi-trauma, and extensive surgery, though one could hypothesize that bacterial translocation from the skin, respiratory, and GI tract may be responsible for these elevations.



### Exclusion Criteria for PCT-guided therapy<sup>24</sup>

- Microbiologically documented infections caused by organisms for which a prolonged duration is standard of care (*Pseudomonas*, *Acinetobacter*, *Listeria*, *Legionella*, *Pneumocystis*, *M. tuberculosis*)
- Severe infections due to viruses and parasites with a risk of bacterial translocation (hemorrhagic fever, malaria)
- Infectious conditions requiring prolonged therapy: endocarditis, brain abscess, deep abscess
- Antibiotics already started 48 hours prior to initial PCT value
- Chronic localized infections (i.e. chronic osteomyelitis, mediastinitis, brain abscess)
- Severely immunocompromised patients (HIV with CD4<200, neutropenic with ANC <500, patients on immunosuppressive therapy after solid organ transplantation)
- Cystic fibrosis<sup>25</sup>

### Proposed Use Scenarios:

#### 1) Emergency Department (Figures 1 and 2)

- For patients being discharged from the ED with upper respiratory tract infections and mild lower-respiratory tract infections (CURB 65 = 0-1 pneumonia, mild COPD exacerbations, acute bronchitis, asthma exacerbations) – decision whether or not to discharge on antibiotics based on single PCT level.<sup>19,26</sup> (Figure 1)
- For patients being admitted with suspected lower respiratory tract infections – decision to initiate or withhold antibiotics based on a single PCT level (and a repeat level in 4-6 hours for patients with initial levels <0.25 ng/mL - if patients are still in the ED).<sup>8,19</sup> (Figure 2)
  - i. Recommend use in conjunction with universal respiratory viral PCR panel, urine Streptococcal and Legionella antigens, and sputum cultures (“the diagnostic bundle” similar to Gelfer 2015<sup>13</sup> and Branche 2015<sup>27</sup>), as an aid to rapid de-escalation in non-infected patients and potentially shorten the length of stay (Inpatient Antibiotic Stewardship).

#### 2) Intensive Care Unit (Figure 3)

- Antibiotic de-escalation for patients with severe sepsis and VAP, based on a Day 0 value, with daily follow up levels. Discontinuation recommended for a PCT decrease by  $\geq 80\%$  over the Day 0 value, or to <0.5  $\mu\text{g/L}$ .<sup>28,29</sup>
  - i. Recommend use in conjunction with blood cultures, universal respiratory viral PCR panel, urine Streptococcal and Legionella antigens, and sputum cultures (“the diagnostic bundle” similar to Gelfer 2015<sup>13</sup> and Branche 2015<sup>27</sup>).

#### 3) Inpatient Non-ICU units (Figure 4)

- Antibiotic initiation and de-escalation for patients admitted with moderate severity respiratory infections (CURB-65 = 2-3 pneumonia, COPD exacerbations, URIs), based on a Day 0 value and a Day 2 value. Withhold antibiotics for initial values <0.1-0.25, discontinue antibiotics when PCT <0.25  $\mu\text{g/L}$ .<sup>22,25,30</sup>
  - i. Recommend use in conjunction with blood cultures, universal respiratory viral PCR panel, urine Streptococcal and Legionella antigens, and sputum cultures (“the diagnostic bundle” similar to Gelfer 2015<sup>13</sup> and Branche 2015<sup>27</sup>).

## Tables and Figures

Table 1. Procalcitonin- guided Antibiotic Therapy: RCTs in Adults

		Respiratory Infections		Critical Care		ED	
		n	Reviewed <sup>11</sup>	n	Reviewed <sup>13</sup>	n	Reviewed <sup>9</sup>
1	Albrich 2012 <sup>28</sup> ProREAL	1425					
2	Annane 2013 <sup>49</sup>			58	Y		Y
3	Boudama 2010 <sup>4</sup> PRORATA	394	Y	630	Y		Y
4	Branche 2015	237					
5	Briel 2008 <sup>34</sup>	458	Y				
6	Burkhardt 2010 <sup>35</sup>	550	Y				
7	Christ-Crain 2004 <sup>24</sup>		Y			243	Y
8	Christ-Crain 2006 <sup>25</sup>		Y			302	Y
9	de Jong 2016 <sup>47</sup> SAPS	994		1546			
10	Deliberato 2013 <sup>50</sup>	?		51	Y		Y
11	Drozdo 2013 <sup>53</sup>					117	Y
12	Hochreiter 2009 <sup>36</sup>	43	Y	110			
13	Kristoffersen 2009 <sup>37</sup>	210	Y				
14	Layios 2012 <sup>51</sup>	?		509	Y		Y
15	Liu 2013 <sup>52</sup>			82	Y		
16	Long 2009 <sup>38</sup>		Y			127	
17	Long 2011 <sup>30</sup>		Y			156	
18	Long 2014 <sup>42</sup>	169					
19	Najafi 2015 <sup>44</sup>			60			
20	Nobre 2008 <sup>39</sup>	59	Y	68			Y
21	Oliveira 2013 <sup>40</sup>			94			
22	Qu 2012 <sup>48</sup>			71	Y		Y
23	Roh 2010 <sup>54</sup>	122	Y			122	Y
24	Roh 2013 <sup>55</sup>	164	Y			164	Y
25	Schroeder 2009 <sup>36</sup>	8	Y	27			
26	Schuetz 2009 <sup>23</sup> ProHOSP	1359	Y			1359	
27	Shehabi 2014 <sup>43</sup>			394			
28	Stolz 2007 <sup>26</sup>	208	Y				
29	Stolz 2009 <sup>27</sup>	101	Y	101	Y		
30	Tang 2013 <sup>41</sup>	258				258	Y
31	Verduri 2015 <sup>45</sup>	178					
32	Wang 2016 <sup>46</sup>	188					
	<b>TOTAL</b>	<b>7125</b>		<b>3700</b>		<b>1231</b>	

Table 2. Role of Procalcitonin levels in the interpretation of clinical microbiology data in patients with lower respiratory tract infections. (Adapted from Gilbert DN, *J Clin Micro* 48(7): 2325-2329.)

Bacterial pathogen detected	Viral pathogen detected	Procalcitonin level (ng/mL)	Interpretation
No	No	$\leq 0.05$	No evidence of bacterial or viral infection
No	No	0.5-1.00	Innate immunity activated; suspect noncultured bacteria, e.g. oral anaerobic organisms
No	Yes	$\leq 0.05$	Viral infection
No	Yes	0.25-1.0	Dual viral and bacterial infection; failure to identify etiologic bacteria
Yes	Yes	0.25-1.0	Dual infection with virus and bacteria
Yes	No	$\leq 0.05$	Bacterial colonization
Yes	Yes	$\leq 0.05$	Bacterial colonization and viral infection

Figure 1. ED Procalcitonin Algorithm – Low Acuity Respiratory Infections

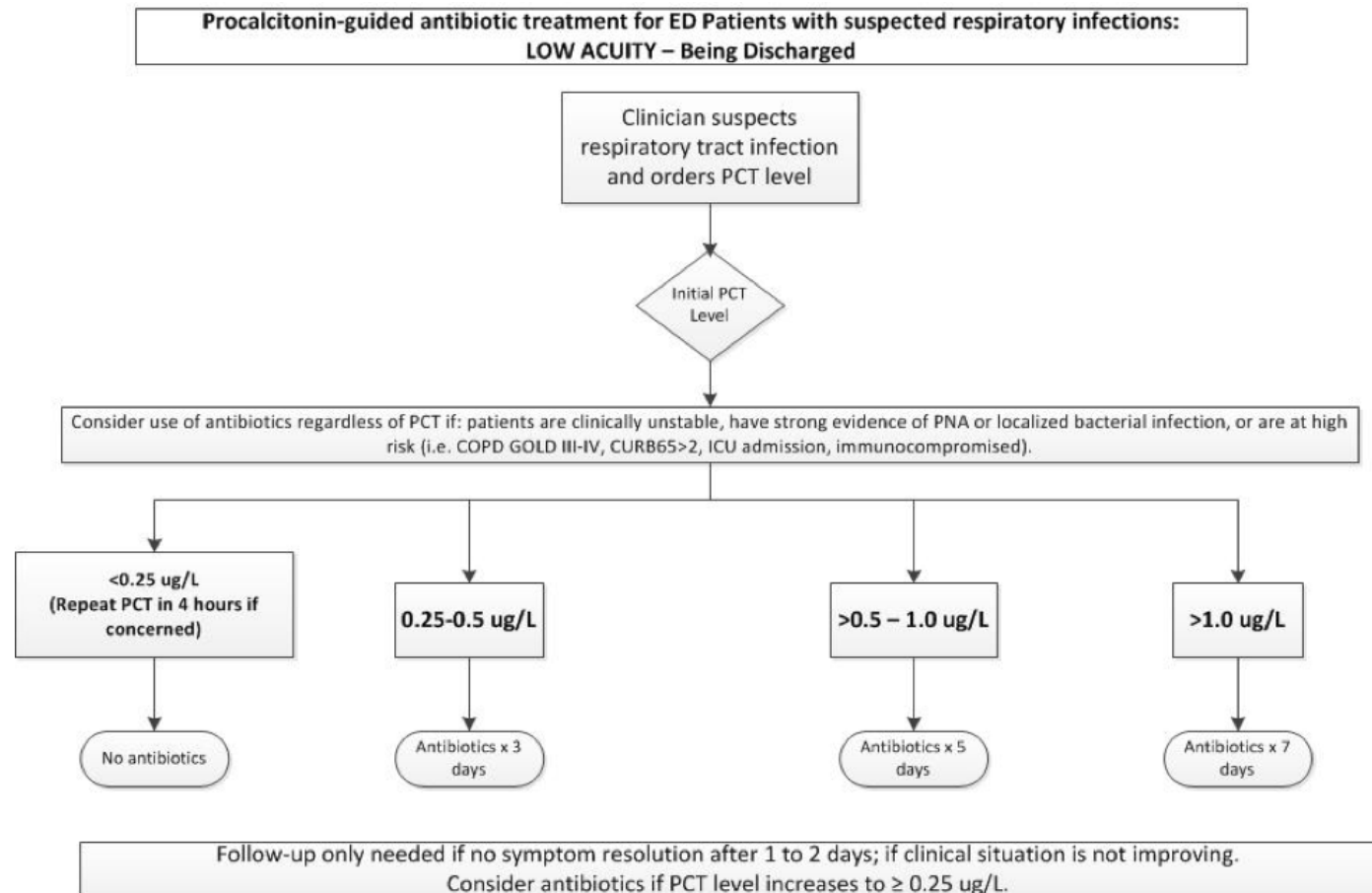


Figure 2. ED Procalcitonin Algorithm – Moderate Acuity Respiratory Infections

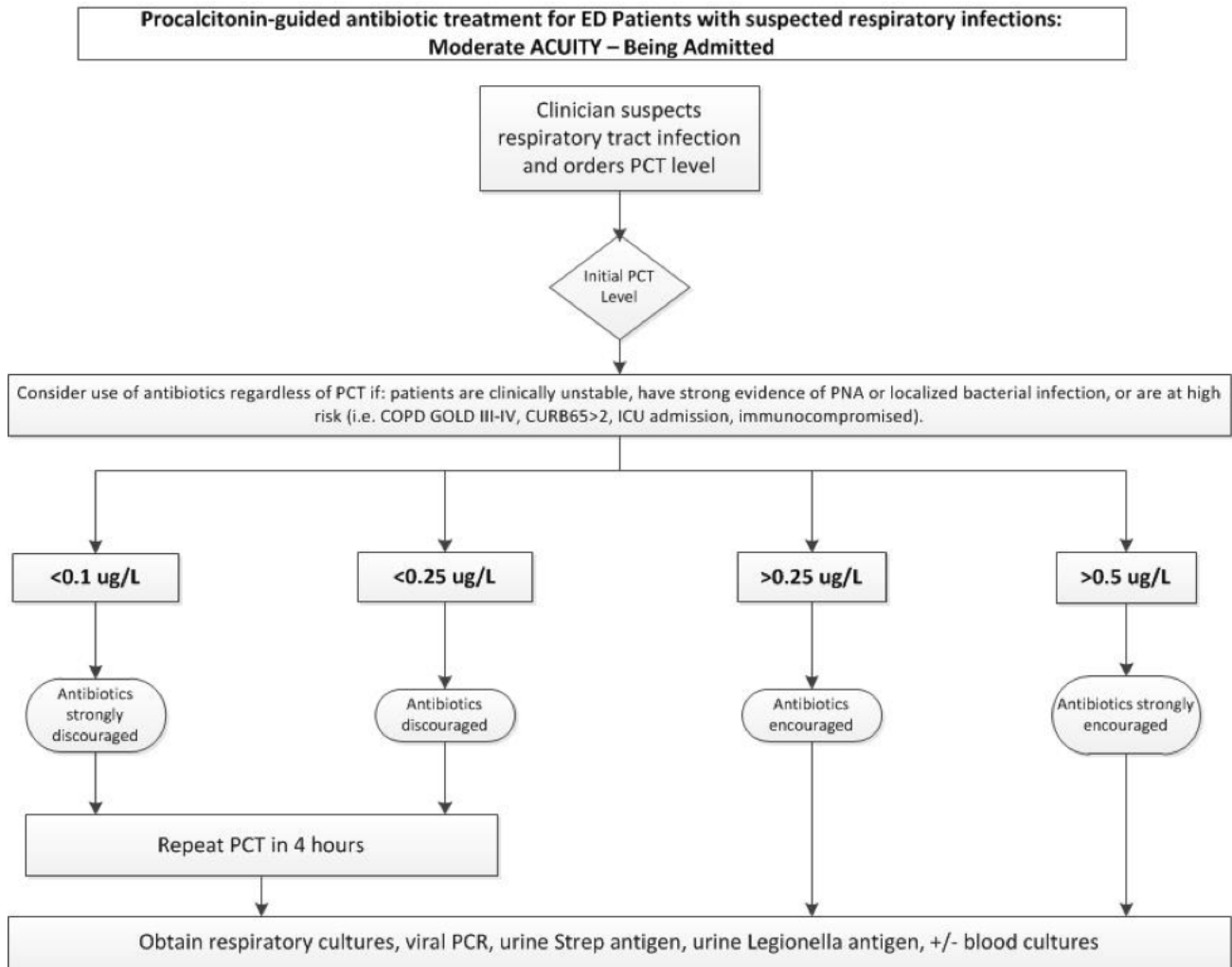
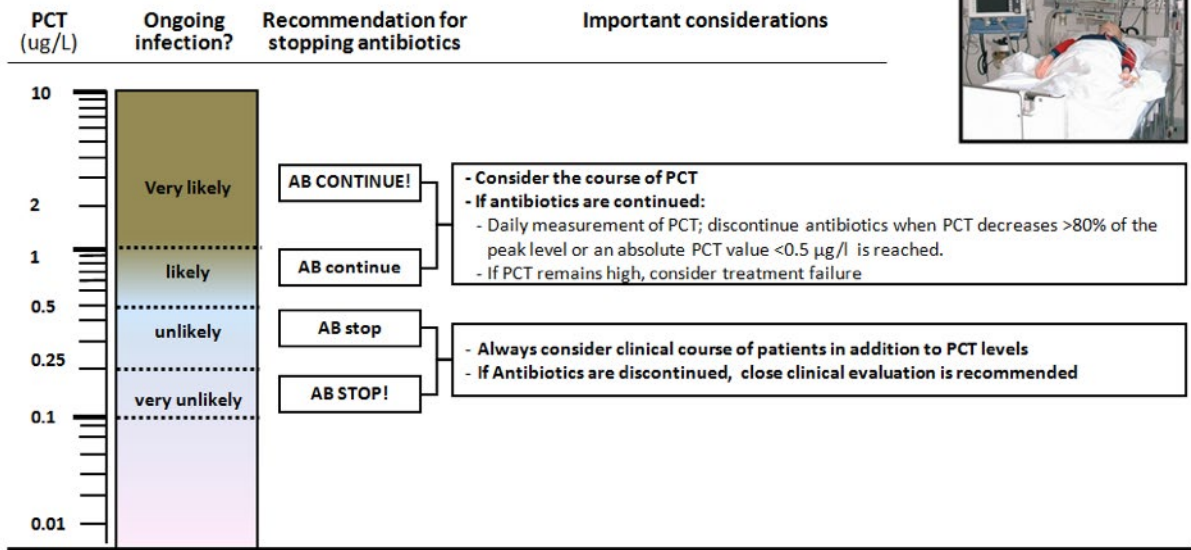


Figure 3. PCT Algorithm for ICU patients, reproduced from Schuetz et al, 2011 with permission.<sup>31</sup>

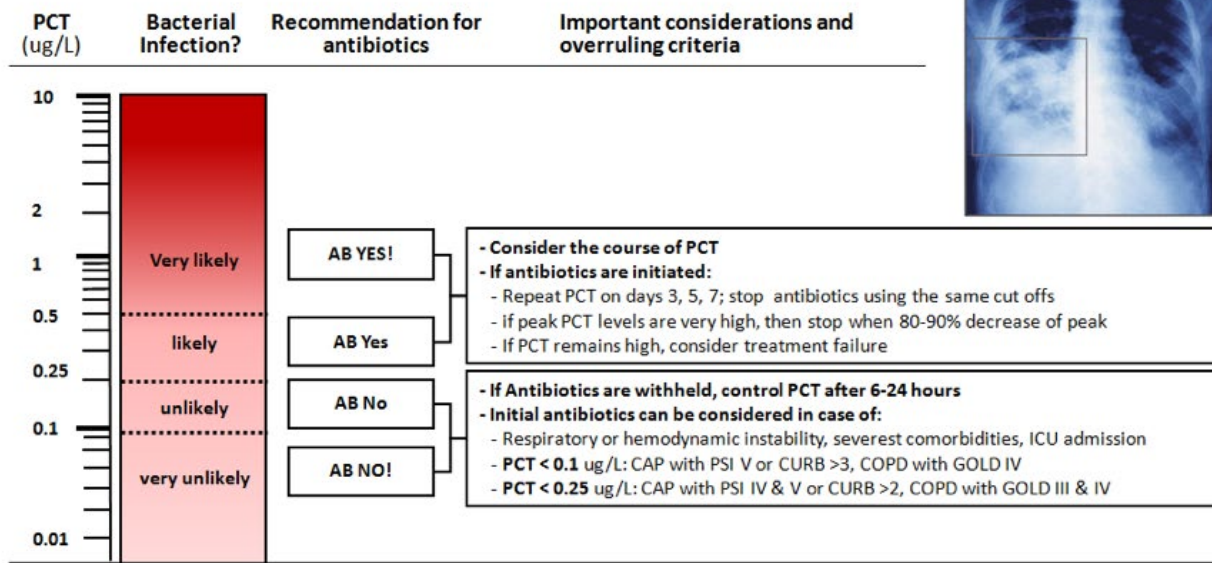
**PCT algorithm for stopping antibiotics in patients with sepsis in the ICU**



PCT algorithm in patients with sepsis in the ICU. In critically ill patients in the ICU, cut-offs are higher and initial empiric antibiotic therapy should be encouraged in all patients with suspicion of sepsis. PCT cut-offs are helpful in the subsequent days after admission to shorten the courses of antibiotic therapy in patients with clinical improvement. Abbreviations: AB, antibiotic; PCT, procalcitonin.

Figure 4. PCT Algorithm for floor patients with respiratory infections, reproduced from Schuetz et al, 2011 with permission.<sup>31</sup>

**PCT algorithm for patients with respiratory tract infection**



PCT algorithm in patients with respiratory tract infections in the Emergency Department. The clinical algorithm for antibiotic stewardship in patients with respiratory tract infections in the Emergency Department encourages (>0.5 µg/L or >0.25 µg/L) or discourages (<0.1 µg/L or <0.25 µg/L) initiation or continuation of antibiotic therapy more or less based on PCT specific cut-off ranges. Abbreviations: AB, antibiotic; LRTI, lower respiratory tract infection; PCT, procalcitonin; PSI, Pneumonia Severity Score

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## Appendix AA: Integration of Procalcitonin with Microbiology Results

The table below is from a mini-review by David Gilbert, MD, Chief of Infectious Diseases at Oregon Health and Science University. Dr. Gilbert is the former president of the IDSA, Co-Chair of the IDSA/FDA Workshop on Clinical Trials of Antimicrobials for Community Acquired Pneumonia, and a member of the Laboratory Diagnostics Task Force of the IDSA. He has advocated the use of procalcitonin in the clinical practice at Oregon for many years and has used it effectively as a stewardship tool in numerous settings including the ICU, Emergency Department, and Medical wards.

Please see his publications for details on his work, referenced below.<sup>1-5</sup>

This 2015 study describes how an ED protocol for evaluation of CAP patients, integrated with procalcitonin results significantly decreased antibiotic use.<sup>1</sup>

This 2010 mini-review describes 4 major uses of PCT in clinical practice that Dr. Gilbert is currently using in Oregon and is the source of the chart below.<sup>2</sup>

Table 1. Role of Procalcitonin levels in the interpretation of clinical microbiology data in patients with lower respiratory tract infections. (Adapted from Gilbert DN, *J Clin Micro* 48(7):2325-2329.)

Bacterial pathogen detected	Viral pathogen detected	Procalcitonin level (µg/mL)	Interpretation
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No	Yes	0.25-1.0	Dual viral and bacterial infection; failure to identify etiologic bacteria
Yes	Yes	0.25-1.0	Dual infection with virus and bacteria
Yes	No	≤0.05	Bacterial colonization
Yes	Yes	≤0.05	Bacterial colonization and viral infection

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## Appendix AB: Sample Antibiotic Time-Outs - Figure 1

Patient Name:		Patient MRN:																
ANTIBIOTICS	Review of Studies		DAY OF THERAPY (check boxes each day if continuing antibiotics)															
	Review daily and complete as data become available		1	2	3	4	5	6	7	8	9	10	11	12	13	14		
antibiotic name / / start date Indication <input type="checkbox"/> Presumed infection -complete yellow box→ <input type="checkbox"/> Surgical prophylaxis (24 hrs.) <input type="checkbox"/> Non-surgical prophylaxis or chronic suppression	Blood Culture <input type="checkbox"/> Positive <input type="checkbox"/> Negative Urine Culture <input type="checkbox"/> Positive <input type="checkbox"/> Negative Resp Culture <input type="checkbox"/> Positive <input type="checkbox"/> Negative Other Micro or Radiology type <input type="checkbox"/> Positive <input type="checkbox"/> Negative	Consider stopping if studies negative 1. Planned duration: ____ days 2. Indication(s): <input type="checkbox"/> Bloodstream <input type="checkbox"/> Neutropenic Fever <input type="checkbox"/> Bone/Joint <input type="checkbox"/> Pelvic/GYN <input type="checkbox"/> C. difficile <input type="checkbox"/> Pneumonia <input type="checkbox"/> CNS <input type="checkbox"/> Respiratory, other <input type="checkbox"/> Endocarditis <input type="checkbox"/> Skin/soft tissue <input type="checkbox"/> Head/Neck <input type="checkbox"/> Urinary tract <input type="checkbox"/> Intra-abdominal <input type="checkbox"/> Other																
			3. Can antibiotic be narrowed based on micro or radiology? →	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>
			4. Can antibiotic be given orally? →	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>
antibiotic name / / start date Indication <input type="checkbox"/> Presumed infection -complete yellow box→ <input type="checkbox"/> Surgical prophylaxis (24 hrs.) <input type="checkbox"/> Non-surgical prophylaxis or chronic suppression	Blood Culture <input type="checkbox"/> Positive <input type="checkbox"/> Negative Urine Culture <input type="checkbox"/> Positive <input type="checkbox"/> Negative Resp Culture <input type="checkbox"/> Positive <input type="checkbox"/> Negative Other Micro or Radiology type <input type="checkbox"/> Positive <input type="checkbox"/> Negative	Consider stopping if studies negative 1. Planned duration: ____ days 2. Indication(s): <input type="checkbox"/> Bloodstream <input type="checkbox"/> Neutropenic Fever <input type="checkbox"/> Bone/Joint <input type="checkbox"/> Pelvic/GYN <input type="checkbox"/> C. difficile <input type="checkbox"/> Pneumonia <input type="checkbox"/> CNS <input type="checkbox"/> Respiratory, other <input type="checkbox"/> Endocarditis <input type="checkbox"/> Skin/soft tissue <input type="checkbox"/> Head/Neck <input type="checkbox"/> Urinary tract <input type="checkbox"/> Intra-abdominal <input type="checkbox"/> Other																
			3. Can antibiotic be narrowed based on micro or radiology? →	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	
			4. Can antibiotic be given orally? →	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	
antibiotic name / / start date Indication <input type="checkbox"/> Presumed infection -complete yellow box→ <input type="checkbox"/> Surgical prophylaxis (24 hrs.) <input type="checkbox"/> Non-surgical prophylaxis or chronic suppression	Blood Culture <input type="checkbox"/> Positive <input type="checkbox"/> Negative Urine Culture <input type="checkbox"/> Positive <input type="checkbox"/> Negative Resp Culture <input type="checkbox"/> Positive <input type="checkbox"/> Negative Other Micro or Radiology type <input type="checkbox"/> Positive <input type="checkbox"/> Negative	Consider stopping if studies negative 1. Planned duration: ____ days 2. Indication(s): <input type="checkbox"/> Bloodstream <input type="checkbox"/> Neutropenic Fever <input type="checkbox"/> Bone/Joint <input type="checkbox"/> Pelvic/GYN <input type="checkbox"/> C. difficile <input type="checkbox"/> Pneumonia <input type="checkbox"/> CNS <input type="checkbox"/> Respiratory, other <input type="checkbox"/> Endocarditis <input type="checkbox"/> Skin/soft tissue <input type="checkbox"/> Head/Neck <input type="checkbox"/> Urinary tract <input type="checkbox"/> Intra-abdominal <input type="checkbox"/> Other																
			3. Can antibiotic be narrowed based on micro or radiology? →	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	Y <input type="checkbox"/> N <input type="checkbox"/>	
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Final diagnoses requiring antibiotics →			Pertinent Positive Microbiology:															
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## Appendix AB: Sample Antibiotic Time-Outs

### Empiric Antibiotic Recommendations

The following are empiric recommendations in absence of culture data. Narrow antibiotics based on culture when available.

#### Urinary Tract Infections

Empiric Antibiotic Choices			
Clinical Setting	Route	Preferred Therapy	Therapy for β-lactam allergy
Uncomplicated Community-Acquired Cystitis <sup>1</sup> (Hospitalized ≤48 hrs)	ORAL		
	IV		
Uncomplicated Hospital-Acquired Cystitis <sup>3</sup> (Hospitalized ≥48 hrs)	ORAL		
	IV		
Complicated Community-Acquired Cystitis <sup>2</sup> AND Pyelonephritis (Hospitalized <48 hrs)	ORAL		
	IV		
Complicated Hospital-Acquired Cystitis <sup>2</sup> AND Pyelonephritis (Hospitalized ≥48 hrs)	ORAL		
	IV		

Duration of Antibiotic Therapy*			
Antibiotic	Uncomplicated Cystitis <sup>1</sup>	Complicated Cystitis <sup>2</sup>	Pyelonephritis
Beta-lactams	3-7 days	10-14 days	10-14 days
Fosfomycin	Single dose	Not recommended	Not recommended
Levofloxacin	3 days	5-7 days	5-7 days
Nitrofurantoin	5 days	Not recommended	Not recommended
Trimethoprim-sulfamethoxazole	3 days	14 days	14 days

<sup>1</sup>In order for cystitis to be considered uncomplicated, none of the criteria for complicated infection can be present (see below)

<sup>2</sup>In order for cystitis to be considered complicated, only one of the following needs to be present: male, urinary catheter within last 48 hrs, fever, urinary tract abnormality, elevated systemic WBC count, pregnancy, renal failure, diabetes or immunosuppression

\*When duration is given as a range, choose duration based on severity of infection AND rate of clinical improvement

#### Pneumonia

Empiric Antibiotic Choices			
Clinical Setting	Route	Preferred Therapy	Therapy for β-lactam allergy
Community-Acquired <sup>1</sup> (patient does not require ICU admission)	IV		
	ORAL		
Community-Acquired <sup>1</sup> (patient requires ICU admission)	IV		
	ORAL		
Healthcare or Hospital-Associated <sup>2</sup> OR Ventilator-Associated <sup>3</sup>	IV		
	ORAL		

Duration of Antibiotic Therapy	
Type	Duration*
Community-Acquired (not MRSA, Legionella or Pseudomonas)	5 days for levofloxacin 750 mg and azithromycin; 7-14 days for other antibiotics
Healthcare, Hospital, or Ventilator-Associated (not MRSA, Legionella or Pseudomonas)	8 days
Legionella pneumophila	7-10 days
MRSA	7-21 days
Pseudomonas aeruginosa	14-21 days

<sup>1</sup>Symptom onset ≤ 48 hrs from admission; <sup>2</sup>Symptom onset ≤ 48 hrs from admission or at another healthcare facility prior to admission; <sup>3</sup>On ventilator w/in 48 hrs of symptom onset.

#### Skin and Soft Tissue Infections

Empiric Antibiotic Choices			
Type	Route	Preferred Therapy	Therapy for β-lactam allergy
Cellulitis, uncomplicated (not critically ill, no abscess)	ORAL		
	IV		
Cellulitis with furuncle, carbuncle, or abscess (does not include after abdominal surgery)	ORAL	+ incision, drainage, culture	+ incision, drainage, culture
	IV	+ incision, drainage, culture	+ incision, drainage, culture
Diabetic foot	ORAL		
	IV		

Duration of Antibiotic Therapy	
Type	Duration*
Cellulitis	5-10 days
Diabetic foot	7-14 days

Antibiotic time-out tools come in many shapes and sizes, and one size does not fit all. A time-out can be guided by a paper form, as shown in Figure 1 in the time-out developed by the University of Pennsylvania stewardship team. The team published a paper showing success with this tool.<sup>1</sup>

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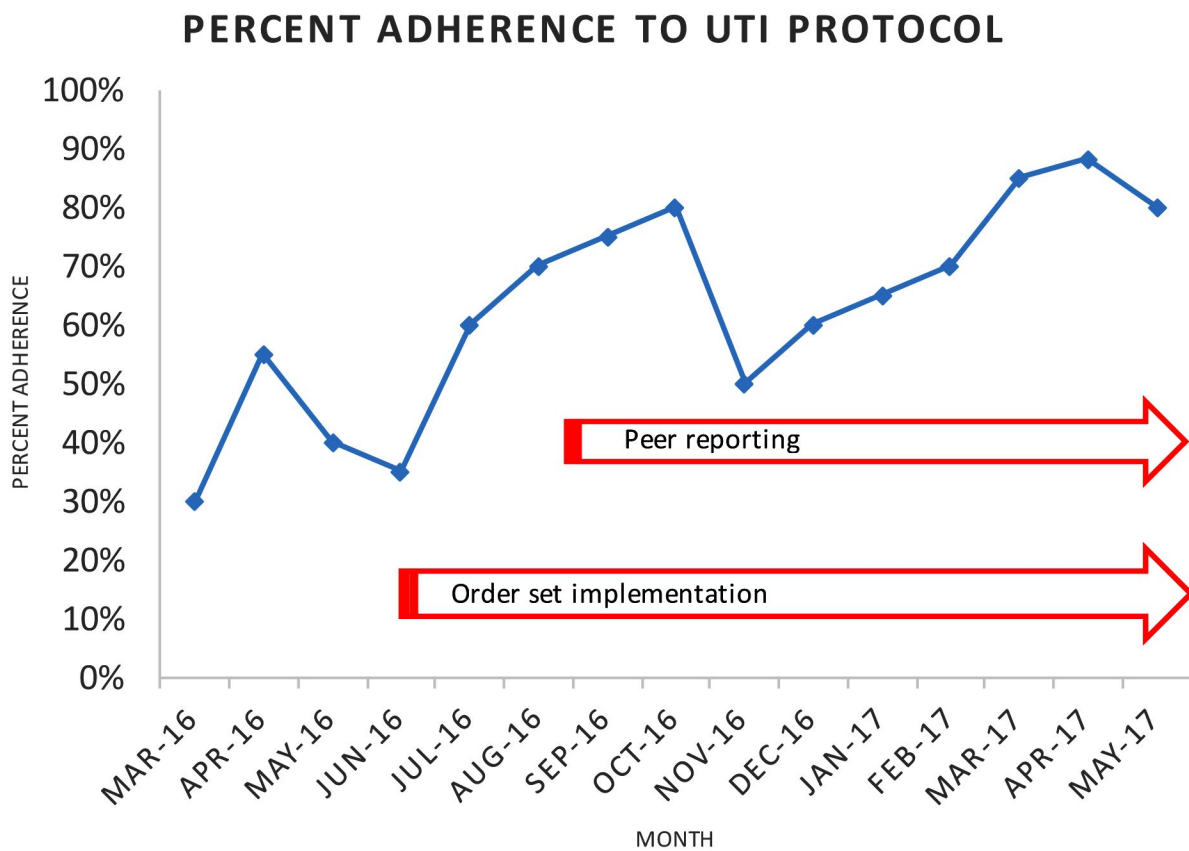
## Appendix AC: Sample Run Chart

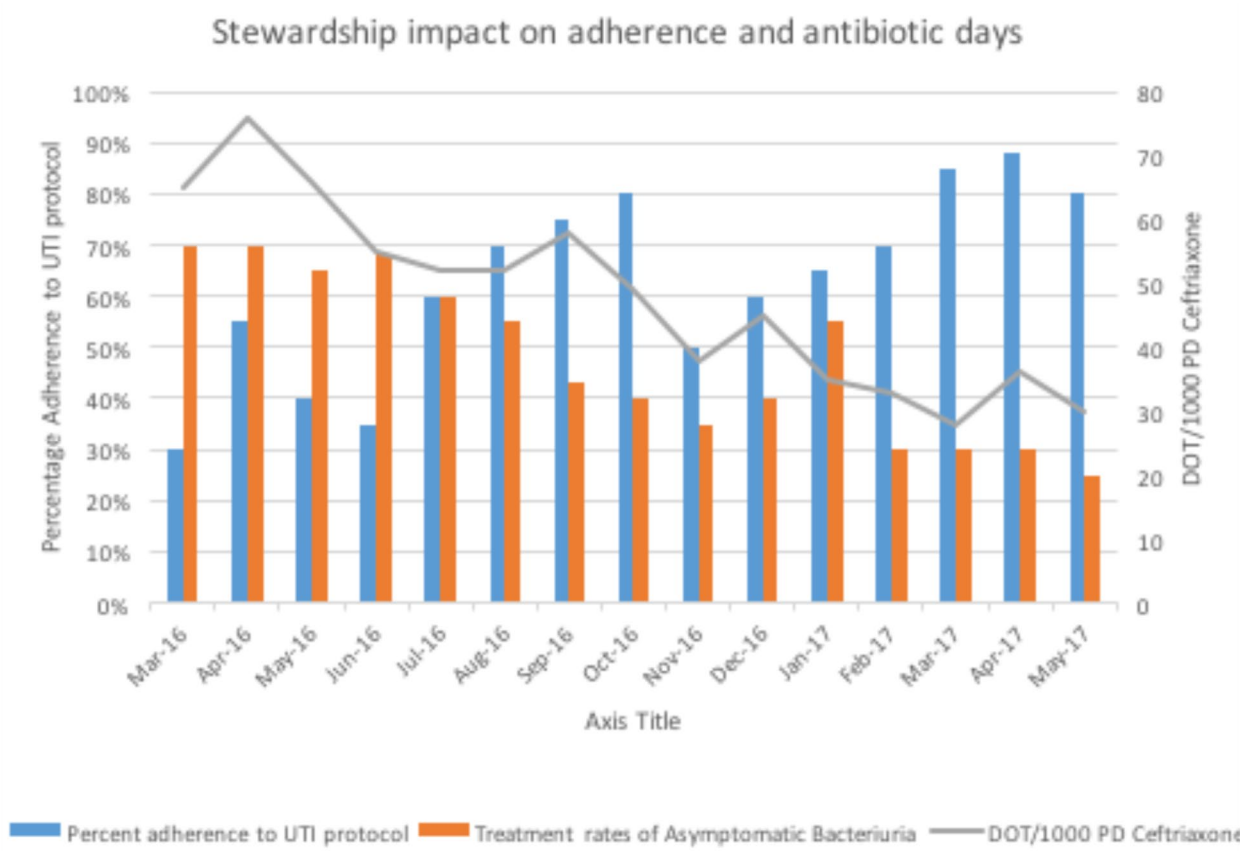
A run chart should summarize progress of your chosen metric over time. See Section IV for information on stewardship metrics.

Keep track of intervention dates so they can be plotted alongside your metrics, to see which interventions are most effective.

Sample 1: Single outcome run chart – process measure of protocol adherence

Sample 2: Multiple outcome run chart – process measure (protocol adherence), plotted alongside treatment rates of asymptomatic bacteriuria as well as ceftriaxone usage (right axis). (FYI: this is fictional chart for illustration purposes only and far more successful than is likely in real life!)



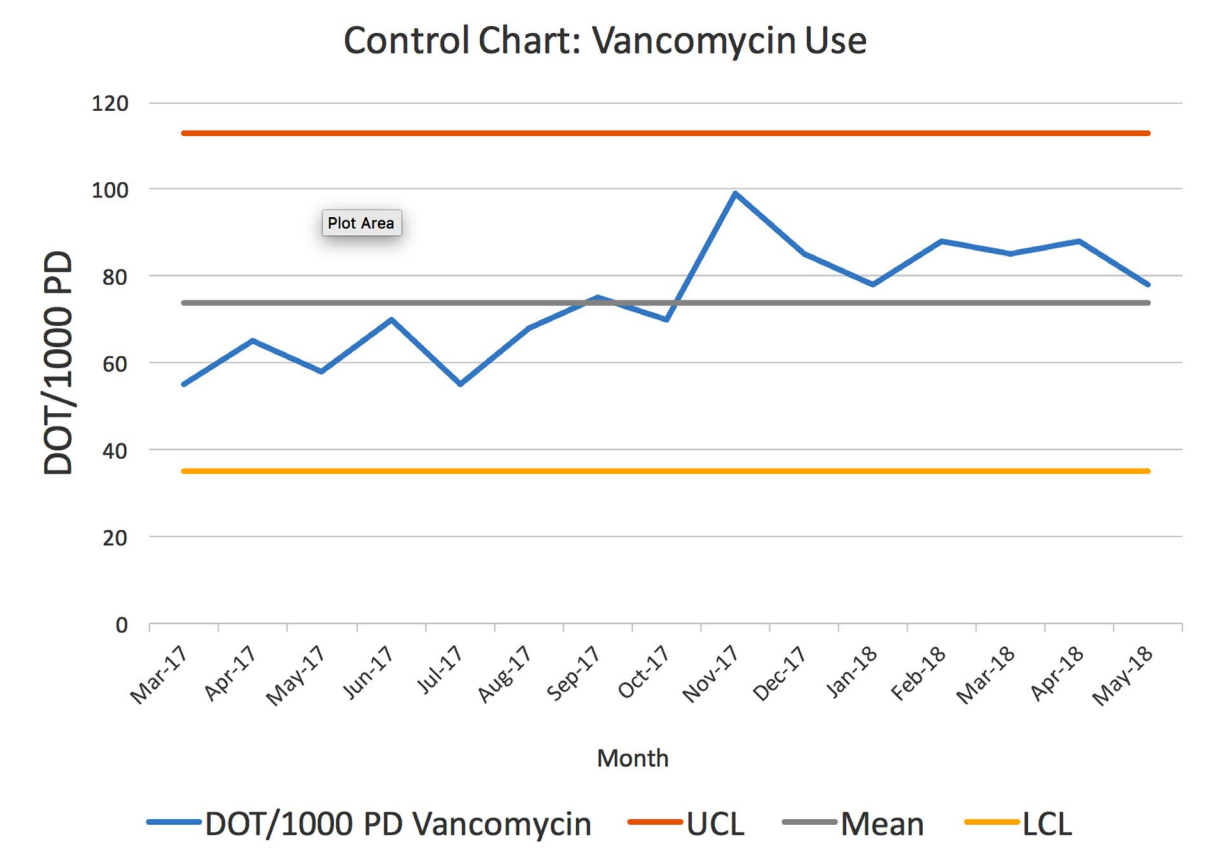


## Appendix AD: IHI Statistical Process Control Chart

Measurement data from healthcare processes display natural variation which can be modelled using a “control chart.” A control chart consists of a series of measurements over time plotted between 2 lines representing the natural random variation of the process. The upper control limit (UCL) and the lower control limit (LCL) are calculated from the inherent variation in the data and are typically set at 2-3 standard deviations (SD) above and below the mean, respectively (statisticians recommend 3 SD). The center line is the mean. If multiple data points begin to fall outside these control limits, one can conclude that a special intervention has caused a significant change.

“Control charts (tools of SPC) can often yield insights into data more quickly and in a way more understandable to the lay decision maker than traditional statistical methods.”<sup>1</sup>

Example using vancomycin days of therapy/1000 PD. Given the wide range in variation in vancomycin use at baseline, an intervention would need to have a huge impact to see a significant change by this method. Ways to decrease the variation would be to separate out the winter months which tend to have more admissions for sepsis, and compare to following winters.



1. Benneyan JC, Lloyd RC, Plsek PE. Statistical process control as a tool for research and healthcare improvement. *Qual Saf Health Care*. 2003;12(6):458-464.

## Appendix AE: Approaches to Penicillin Allergy

### Background:

Up to 10% of the population report an allergy to penicillin, but <1% of people are truly allergic. **Antibiotics given for penicillin allergic patients are often unnecessarily broad, expensive and less effective antibiotics** (i.e., vancomycin for MSSA).<sup>1</sup> These patients are at **higher risk for C. diff and drug-resistant infections, and have longer length of stay.**<sup>2</sup> De-labeling patients with fallacious allergies is a stewardship priority and can lead to cost savings. The key is to determine if the patient had an IgE-mediated reaction or another serious hypersensitivity that would contraindicate future penicillin use.

Tools for de-labeling patients with penicillin allergies include 1) taking a history to elicit possible IgE mediated (high-risk) reactions, 2) skin testing, 3) desensitization of patients with IgE-mediated reactions and 4) drug challenges (test dose or graded challenge) for patients with low-risk histories (primarily delayed-onset rashes) when skin testing is not available. See the CDC recommendations below, as well as the articles listed, for different integrated approaches based on facility resources. The approaches are listed in order of increasing complexity.

Table 1. Features of IgE Mediated Reactions

IgE Mediated Reaction	Comment
Reactions occurs immediately (usually within 1 hour)	Can happen up to 6 hours later
Wheezing and shortness of breath	
Angioedema	Localized edema without hives (abdomen, face, extremities, genitals, oropharynx, larynx)
Hives	Multiple red/raised/itchy papules that come and go
Anaphylaxis (2 systems affected)	Skin, respiratory, cardiovascular (including tunnel vision/ impending doom), GI

Table 2. Severe (non-IgE) Drug Hypersensitivity Reactions

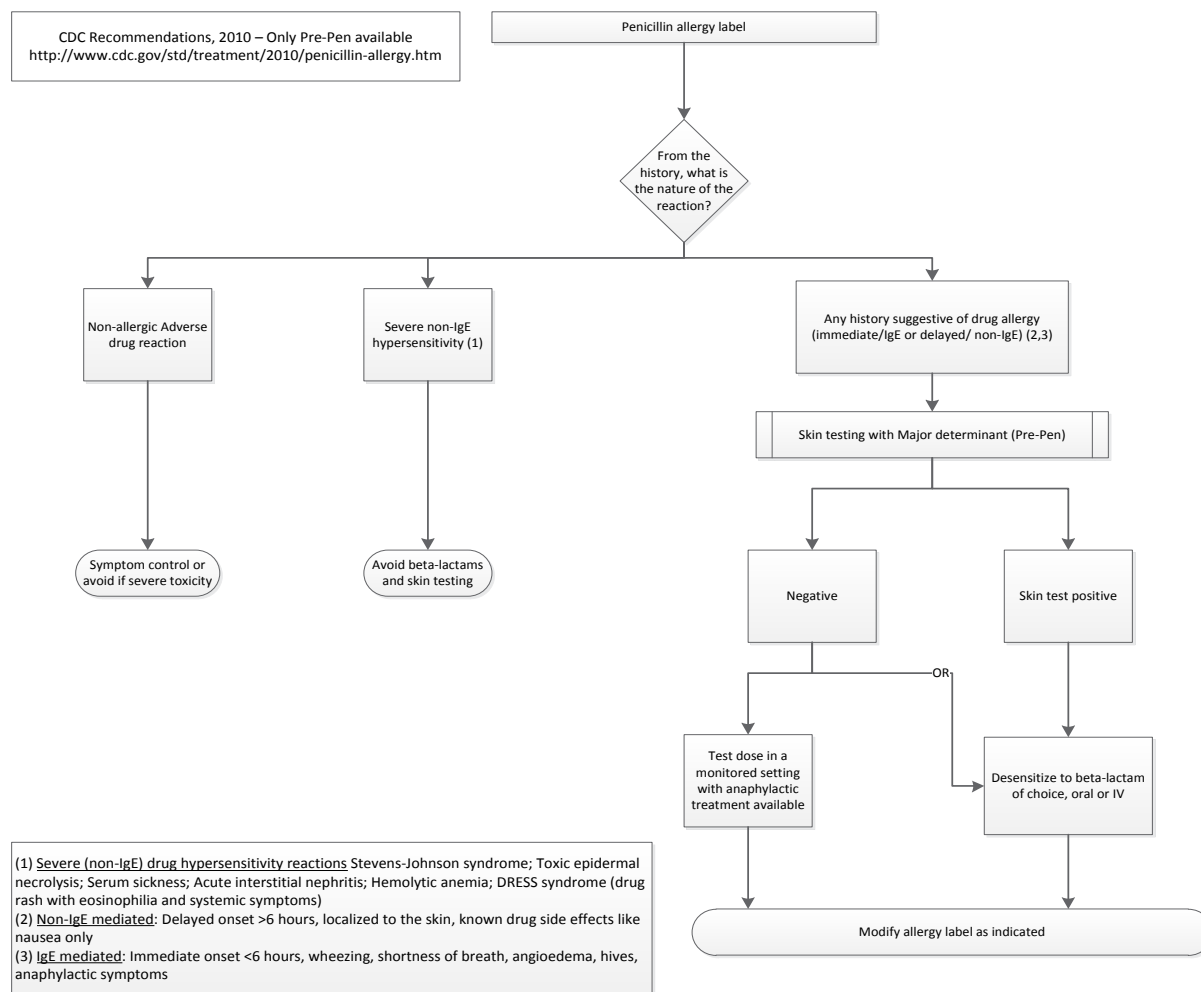
Stevens-Johnson syndrome
Toxic epidermal necrolysis
Serum sickness
Acute interstitial nephritis
Hemolytic anemia
DRESS syndrome (drug rash with eosinophilia and systemic symptoms)

## Basic Approach: The CDC Approach – No skin testing available (Figure 1)

[<http://www.cdc.gov/std/treatment/2010/penicillin-allergy.htm>]

If no skin testing is available, the facility should use the CDC recommendations for this circumstance, using a test dose for low-risk patients and desensitization of high-risk patients. A sample test dose procedure is to give 1/10th of the full IV dose, or 1/4th of a pill of the chosen antibiotic and monitor for 2 hours.

## Intermediate: The CDC Approach – Pre-Pen (Figure 2)

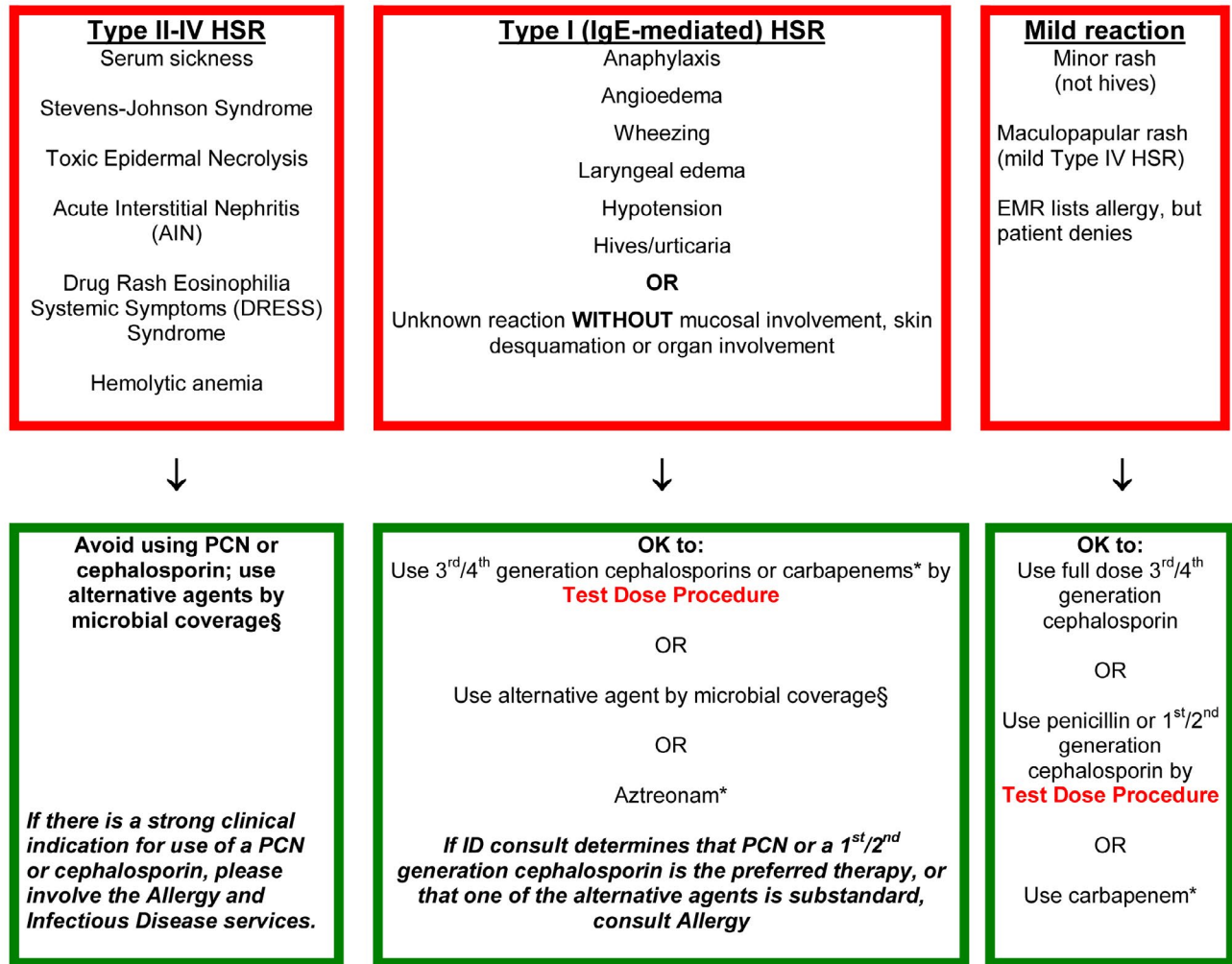


Pre-Pen is an easy-to-use penicillin skin-testing device that contains only the major determinants of penicillin (<http://www.pre-pen.com/>). It can be administered by a trained nurse practitioner. A negative test reduces the chances of an immediate-type IgE reaction to <5%. Because truly allergic patients can experience anaphylaxis with testing, it must be done in a monitored setting with epinephrine and steroids on hand.



**Advanced: The Massachusetts General Hospital Strategy<sup>3-5</sup> (Figure 3)**

For a printable version of Figure 1 click here.



§ ALTERNATIVE AGENTS BY MICROBIAL COVERAGE (see Table 1 for additional details):  
**Gram positive coverage:** Vancomycin, linezolid\*, daptomycin\*, clindamycin, doxycycline, TMP/SMX  
**Gram negative coverage:** Quinolones, sulfamethoxazole / trimethoprim, aminoglycosides, carbapenems\*, aztreonam\*

**Cephalosporins by class available on the MGH Formulary:**  
 1<sup>st</sup>cephalexin/cefazolin • 2<sup>nd</sup>cefotixin/cefuroxime  
 3<sup>rd</sup>ceftriaxone/cefixime/cefotaxime/cefopodoxime/ceftazidime\* • 4<sup>th</sup>cefepime • 5<sup>th</sup>ceftaroline\*

HSR: Hypersensitivity Reaction  
 \* ID approval required either by the Antibiotic Approval Pager or by ID Consult Service

A targeted test-dose approach for inpatients has been developed by the Allergy group at Massachusetts General Hospital. The group has evaluated multiple testing and treatment strategies and has found the algorithm (Figure 3) to be safe and effective for inpatients.<sup>4,5</sup> Their algorithm gives recommendations for use of cephalosporins and carbapenems in IgE mediated reactions. Instead of skin testing, they recommend an Allergy Consult for patients with an IgE mediated reaction who need to use penicillins or 1st/2nd generation cephalosporins.

After they implemented this protocol hospital wide in 2013, there was a seven-fold increase in the number of test doses done and a decrease in alternative antibiotic use (vancomycin, aztreonams, quinolones) without an increase in adverse drug reactions (drug reactions occurred in 7/183 or 4% post guideline).<sup>4</sup>

The details of the test dose procedure, penicillin pathway and cephalosporin pathway are available in the online supplement of the 2014 Blumenthal article.<sup>3</sup> An app is also forthcoming at the end of 2016.

### **Additional information:**

Drug Allergy: An Updated Practice Parameter. Joint Task Force on Practice Parameters. *Ann Allergy Asthma Immunol.* 2010;105(4):259-273.

### Test Dose Procedure

Please print the [Test Dose Procedure](#) and place in chart for Nursing staff.

The **Test Dose**, as recommended by the **MGH Penicillin and Cephalosporin Hypersensitivity Pathways** is a safe procedure that can be performed by primary teams on a general hospital ward. We currently recommend test doses when patients have a low risk of reaction. If the patient tolerates both the test dose and full dose, then this would confirm that the patient can tolerate the drug without developing a Type I (IgE-mediated) hypersensitivity or other allergic reactions that have been determined to be minor.

#### Place the following orders in POE prior to Test Dose Procedure:

1. If possible, hold the following medications the day of the Test Dose Procedure:
  - a. Beta blockers: inhibit the action of epinephrine.
  - b. ACE inhibitors: increase the risk of an allergic reaction.
2. RN to record vital signs (blood pressure, heart rate, and respiratory rate) prior to administering the drug (time 0) and every 30 minutes from the start of the procedure to the end of the procedure (time 120 minutes).
3. Write for the following PRN medications to be at the patient's bedside:
  - a. Epinephrine 1:1000 for intramuscular administration (0.3 mg)
  - b. Benadryl 50 mg for IV/PO administration
4. Order: Medication Order:
  - a. Calculate and order 1/10 of the intended treatment dose for an IV medication or ¼ of a pill for an oral medication. Indicated in the instructions for this order that this dose is for step 1 of the Test Dose Procedure per the **MGH Penicillin and Cephalosporin Hypersensitivity Pathway**.
  - b. One dose of the full treatment dose. Indicate in the instructions for this order that this dose is for step 2 of the Test Dose Procedure per the **MGH Penicillin and Cephalosporin Hypersensitivity Pathway**.

*Note: orders will only be processed by pharmacy if this is included in the order.*

#### Test Dose Procedure:

- Step #1: The RN administers test dose as per orders above. RN records vital signs just prior to administration of test dose. At 30 minutes later, the RN checks vital signs and makes sure that the patient has not developed any rash or other symptoms. RN repeats vital signs and evaluation at 60 minutes (from initial test dose). If the patient remains asymptomatic and vital signs remain normal the RN may proceed to step #2.
  - Step #2: The RN administers the full intended treatment dose of the medication. At 30 minutes later, the RN checks vital signs and makes sure that the patient has not developed any rash or other symptoms. RN repeats vital signs and evaluation at 60 minutes (from full treatment dose). If the patient remains asymptomatic and vital signs remain normal, then the patient will have successfully completed the test dose procedure without any reaction and can subsequently receive the medication as scheduled by the team.
- If a reaction occurs as a consequence of this procedure, please page the allergy fellow on call (p13042) and complete an Incident Report.
- Please document any appropriate changes in allergy status once Test Dose Procedure is completed.

Signature \_\_\_\_\_

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# Fight The RESISTANCE

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The RESISTANCE

