ACKNOWLEDGEMENTS

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Accessible at: http://www.hret-hiin.org/

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How to Use Your Change Package

This change package is intended for hospitals participating in the Hospital Improvement Innovation Network (HIIN) project led by the Centers for Medicare & Medicaid Services (CMS) and Partnership for Patients (PFP); it is meant to be a tool to help you make patient care safer and improve care transitions. This change package is a summary of themes from the successful practices of high-performing health organizations across the country. It was developed through clinical practice sharing, organization site visits and subject matter expert contributions. This change package includes a menu of strategies, change concepts and specific actionable items that any hospital can implement based on need or for purposes of improving patient quality of life and care. This change package is intended to be complementary to literature reviews and other evidence-based tools and resources.
DEFINITION: The Infectious Disease Society of America defines antibiotic stewardship as “coordinated interventions designed to improve and measure the appropriate use of antimicrobials by promoting the selection of the optimal antimicrobial drug regimen, dose, duration of therapy, and route of administration. Antimicrobial stewards seek to achieve optimal clinical outcomes related to antimicrobial use, minimize toxicity and other adverse events, reduce the costs of health care for infections, and limit the selection for antimicrobial resistant strains.”

Magnitude of the Problem — Why this Matters

Even before penicillin was released in 1943, Sir Alexander Fleming noted that resistance to it had already emerged. He warned that the "public will demand [the drug and] ... then will begin an era ... of abuses." Resistance has since extended to virtually every antibiotic. The causes are multiple: natural abilities of bacteria to mutate and evolve into resistant strains, sharing of resistance capabilities amongst bacteria of the same or different species, and overuse and abuse of antibiotics. Studies show that between 30-50% of both inpatient and outpatient antibiotic prescriptions either are unnecessary or erred in drug, dose, or duration. Furthermore, development of new classes of antibiotics that work through novel mechanisms has dramatically slowed. The Centers for Disease Control and Prevention (CDC) reports that drug-resistant bacteria cause 23,000 deaths and 2 million illnesses each year. Avoidable costs from antibiotic misuse range from $27 billion to $47 billion per year in the United States.

To help promote responsible antibiotic stewardship, the CDC released in 2014 a document detailing the seven Core Elements of hospital antibiotic stewardship programs. The National Quality Forum has published a “Playbook” that aligns with the CDC Core Elements and provides a practical approach to developing an effective antibiotic stewardship program (ASP) that details strategies and offers suggestions for successful implementation.

A survey performed by the National Healthcare Safety Network (NHSN) of acute care hospitals in the United States later that year revealed that implementation of ASPs varies widely across the nation. Of note, while hospitals with greater than 200 beds were more likely to have an ASP, 25% of hospitals with 50 beds or fewer reported meeting all seven core elements. While the survey showed that hospitals of all sizes in all states can develop and implement effective ASPs, the survey revealed that only 39% of hospitals have an ASP that meets all seven core elements. The importance of effective ASPs has been underscored by The Joint Commission, which published a new Antimicrobial Stewardship Standard in 2016.
PART 2: MEASUREMENT

A key component in making patient care safer in your hospital is to track your progress toward improvement. Collecting data points at your hospital will guide your quality-improvement efforts as part of the Plan-Do-Study-Act (PDSA) process. Tracking your data in this manner will provide valuable information needed to study your data across time and help determine the impact of your improvement initiatives on reducing patient harm.

Nationally Recognized Measures: Process

Please download and reference the Encyclopedia of Measures (EOM) on the HRET HIIN website for additional measure specifications and for any updates after publication at: http://www.hret-hiin.org/resources/display/encyclopedia-of-measures-eom

Consider the process measures below for measuring the effectiveness of ASPs. Examples of those in use that are supported by evidence include:

> Process Measures:

  - **Basic:**
    - Document of indication for each antibiotic start
    - Performance of time-outs, along with tracking of diagnosis, drug, dose, duration, and de-escalation with antibiotic time-out
    - Adherence to facility-specific treatment recommendations or guidelines for antibiotic prescribing
    - Accurate antibiotic allergy and adverse reaction histories

  - **Advanced:**
    - Days of Therapy (DOT): Number of antibiotics administered per patient per day
    - Defined Daily Dose (DDD): Grams of antibiotics used (if DOT data not available)
    - Standardized Antibiotic Administration Ratio (SAAR)

PART 3: APPROACHING YOUR AEA

> Suggested Bundles and Toolkits:

• The HRET HIIN Antibiotic Stewardship Top Ten Checklist [See Appendix I]


Investigate Your Problem and Implement Best Practices

DRIVER DIAGRAMS: A driver diagram visually demonstrates the causal relationship between your change ideas, secondary drivers, primary drivers, and overall aim. A description of each of these components is outlined in the table below. This change package reviews the components of the driver diagram to help you and your care team identify potential change ideas and to show how this quality-improvement tool can be used by your team to tackle new process problems.
### AIM

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<th>PRIMARY DRIVER</th>
<th>SECONDARY DRIVER</th>
<th>Change Idea</th>
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<tr>
<td>AIM: A clearly articulated goal or objective describing the desired outcome. It should be specific, measurable and time-bound.</td>
<td>PRIMARY DRIVER: System components or factors that contribute directly to achieving the aim.</td>
<td>SECONDARY DRIVER: Action, interventions or lower-level components necessary to achieve the primary driver.</td>
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### Drivers in This Change Package

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<td>Develop Communication Plan</td>
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<th>Establish Capacity, Capability, and Accountability</th>
<th>Establish Program Governance</th>
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<td>Provide Clinician Training, Education, and Certification</td>
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<th>Match the Drug to the Bug</th>
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<td>Standardize Timely Culture &amp; Sensitivity Review</td>
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<td>Apply Stewardship Techniques</td>
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<td>Know When and How to Say &quot;No&quot;</td>
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<th>Aim, Measure, Analyze, and Report</th>
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<th>Engage Patients and Families</th>
<th>Use Multiple Modalities to Teach Risks and Appropriateness</th>
<th>Change Ideas</th>
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<tr>
<td>Teach What to Do If Antibiotics Are Ordered</td>
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Primary Driver: CREATE ORGANIZATIONAL WILL

Many challenges currently face leaders, managers, and clinicians. Development and implementation of an effective ASP requires an understanding of the growing problem of antibiotic resistance, the significance of the volume of inappropriate antibiotic prescribing, and evidence that proven effective means to address these issues exist. Organizational will leads to commitment and focus, which is required for successful ASP implementation.

An effective ASP provides better patient care and reduces costs, many of which are large savings to the hospital.¹⁷

Secondary Driver > SECURE VISIBLE LEADERSHIP COMMITMENT

"To succeed, antibiotic stewardship programs need clear support from hospital leadership. Leadership commitment can be demonstrated in many ways, and the board, executive team, leadership, and professional staff must all clearly support that commitment."¹⁸ The NHSN survey described above found that written leadership support was highly correlated (7-fold increase) with having a comprehensive ASP. Written leadership support, formal statements and clear communication strategies; paid education and training opportunities; sustained financial support; and time to perform the necessary functions are all key elements of successful ASPs.¹⁹

Change Ideas

> Include ASP development and implementation status reports, along with results, to the board at least quarterly.
> Illustrate to leaders the benefits of an ASP through data, narratives, and presentations.
> Support the identification, education, and development of physician and pharmacy ASP champions.
> Illustrate the financial benefits derived from a successful ASP.²⁰, ²¹, ²²

Suggested Process Measures for Your Test of Change

• Presence or absence of formal written statements of ASP support from leadership.
• Amount of financial support committed to ASP development, implementation, and sustainment.

Secondary Driver > PERFORM GAP ANALYSIS

Gap analysis tools can be very effective in helping an organization identify critical areas of a process that has not been addressed, needs more attention, or needs to be spread. The CDC has published a powerful gap analysis tool entitled Antimicrobial Management Program Gap Analysis Checklist.²³ This tool is referenced above in the "Suggested bundles and toolkits" section. The proper process for the use of this tool is to develop a small, multi-disciplinary task force to mindfully work through the tool and compare the organization’s policies, procedures, and practices with optimal ones. It is not a "check the box" exercise. Once the tool has been completed, the results can be used to guide and prioritize next steps.

AIM

DECREASE DAYS OF THERAPY (DOT) BY 20 PERCENT BY SEPTEMBER 27, 2018

Measurement of effectiveness of an antibiotic stewardship program (ASP) can be difficult as many of the suggested outcome measures are either reported infrequently (antibiogram), or are measures loosely associated with an effective ASP (CDI and MRSA rates and clinical outcomes). In lieu of an optimal measure, the CDC, supported by major national organizations, recommends using DOT as a primary measure. While this measure is imperfect, as studies have revealed that approximately 30-50% of both inpatient and outpatient antibiotic use is unnecessary,¹⁵,¹⁶ it provides a useful metric to guide stewardship.
Change Ideas

> Access the checklist and engage a small, multidisciplinary group that includes a physician, pharmacist, nurse, infection preventionist and others who know the true practices of the organization.

> Set aside one to two hours to complete this. If it does not get completed, regroup and complete at another time.

> Communicate the results of the gap analysis to key stakeholders.

> Identify next steps. Start small. Develop competence and confidence.

Suggested Process Measures for Your Test of Change

- The number of physicians present during the analysis of the gap checklist.
- The number of pharmacists present during the analysis of the gap checklist.
- The degree of “buy-in” by key stakeholders after communication of the gap analysis results (qualitative measure).

Secondary Driver > DEVELOP COMMUNICATION PLAN

All significant process changes benefit from well-developed communication plans that enhance staff engagement. Communication should be offered in multiple modalities, from those that share information (e.g., newsletters, posters, emails) to those that shape new behaviors (e.g., face-to-face meetings). Understanding how different individuals and different disciplines are intrinsically motivated and then targeting messaging to answer the “What’s in it for me?” question increase engagement.

Change Ideas

> Consider framing the communication plan positively: “protect selected antibiotics” rather than “restrict” them. [Courtesy of Stephanie Justice, PharmD, St. Claire Regional Medical Center, Morehead, Kentucky]

> Develop a communication plan targeted to physicians regarding the need and effectiveness of an ASP. Lead the communication by linking ASPs to better patient care; leading with financial savings arguments are less likely to engage and motivate physician support.24

> Meet with multidisciplinary groups of staff; seek out and identify champions.

> Listen to concerns, and identify potential barriers, allowing the opportunity to design and integrate mitigation strategies into the implementation plans.

Suggested Process Measures for Your Test of Change

- Survey, formally or informally, the effectiveness of communication strategies.
- Measure attendance at multidisciplinary meetings: are key stakeholders present?

Hardwire the Process

Create and fund a budget item to support protected time for ASP implementation. Add ASP as a regular standing item to board, leadership and clinician meetings. As the program evolves, move the discussion from why, to how, to how are we doing. Regularly seek input regarding successes and barriers to ASP during executive walk rounds.
**Primary Driver:**

**ESTABLISH CAPACITY, CAPABILITY, AND ACCOUNTABILITY**

Leading national organizations strongly recommend that capacity, capability and accountability be established to have an effective ASP. Thus, it is important to ensure that staff have protected time as well as proper knowledge and training. Their actions should then be held accountable by leadership.

**Secondary Driver > ESTABLISH PROGRAM GOVERNANCE**

A leader or co-leaders should be designated to lead the ASP. A physician-pharmacist dyad is optimal. These leaders are responsible for program outcomes.

**Change Ideas**

- Seek physician and pharmacist champions who can serve as collaborative co-leaders.
- Seek champions who are respected among their peers and who have good communication skills.
- Find those with expertise in antibiotics if possible; if not possible, any clinician champion can succeed, especially with additional training (see below).
- Consider appointing a nurse practitioner as a co-leader if a physician does not come forward.

**Suggested Process Measures for Your Test of Change**

- Is there an identified leader or co-leaders who will develop and manage the ASP? (Yes/No)
- Is the leader respected among peers and good at communicating? (Yes/No)
- Do the ASP leaders have protected time to develop and monitor the ASP? (Yes/No)

**Secondary Driver > PROVIDE CLINICIAN TRAINING, EDUCATION, AND CERTIFICATION**

While it might be deemed optimal to have an infectious disease specialist and a pharmacist with special training in antibiotic use as co-leaders, this is not required. Many successful programs have been led by generalists who receive extra training.

**Change Ideas**

- Support training for the ASP leaders.
- Enroll pharmacists in programs offered by the Society of Infectious Disease Pharmacists, found at [http://www.sidp.org/page-1442823](http://www.sidp.org/page-1442823).
- Enroll physicians, pharmacists, and infection preventionists into programs offered by Making A Difference in Infectious Diseases (MAD-ID), found at [http://mad-id.org/antimicrobial-stewardship-programs/](http://mad-id.org/antimicrobial-stewardship-programs/).

**Suggested Process Measures for Your Test of Change**

- Do the ASP leaders have expertise in best practice for antibiotics use and stewardship? (Yes/No)
- If not, have you supported their enrollment in certification programs, and are they completing these programs? (Yes/No)

**Secondary Driver > DEFINE ROLES, RESPONSIBILITIES, AND EXPECTATIONS**

Defining and communicating roles, responsibilities and expectations for an ASP are key. Examples of specific roles, responsibilities, and expectations include:

- Leadership and finance: development of broad goals for the ASP, provision of visible support (documents, rounds, protected time, financial support), monitoring, and assistance with surmounting cross-disciplinary barriers.
> Physicians: engagement with the ASP to improve antibiotic usage practices for better patient outcomes and reduced antibiotic resistance, collaboration with pharmacists and other professionals, education of patients, and resistance to demands for unwarranted antibiotics. “One of the first duties of the physician is to educate the masses not to take medicine.” (Ostler)

> Pharmacists: promotion of the optimal use of antimicrobial agents, reduction of the transmission of infections, education of health professionals, patients, and the public.25

> Infection Preventionists: assistance with prompt detection of multi-drug resistant organisms (MDROs), promotion of compliance with standard and transmission-based precautions, and facilitation of other infection prevention strategies, all of which help reduce healthcare-associated infections, antibiotic usage, and MDROs.26

> Frontline Nurses: ensure pertinent information about antibiotics is available at the point of care, question the antibiotic administration route and duration, reassess antibiotic therapy in 2-3 days, review antibiotic therapy when your patient develops a new C. difficile infection, and reconcile antibiotics during all patient care transitions.27

**Change Ideas**

> Convene a multidisciplinary task force, including leadership and finance, to develop and integrate roles, responsibilities, and expectations, and obtain buy-in amongst peer groups.

> Meet with frontline staff of all disciplines, and discuss these key elements.

> Join a collaborative that is focusing on antibiotic stewardship.

> Consult with other hospitals of similar size and resources to learn from and possibly partner with them.

**Suggested Process Measures for Your Test of Change**

- Survey staff to determine their understanding of their specific role in the ASP.

- Survey the leadership and frontline staff to measure resistance to the new roles and the cause of that resistance.

**Hardwire the Process**

Develop a simple and concise charter that clearly outlines the purpose and scope of the ASP, along with all roles, responsibilities, and expectations. Discuss with staff, and amend as appropriate. Keep these elements top of mind by regularly including the discussion of these items during leadership, medical staff, pharmacy, and frontline nursing meetings and shift huddles.
Primary Driver: 
**MATCH THE DRUG TO THE BUG**

Proper use of antibiotics revolves around several basic questions:

> Does the patient have an infection?
> If the patient has an infection, is it a bacterial infection?
> If it is a bacterial infection, what is the likely source?
> If it is a bacterial infection, are culture and sensitivity (C&S) information available?
> If C&S information is not available, based on the patient’s history or the local antibiogram, is the bacteria likely to be resistant to usual treatment?
> Is the dosage and duration of therapy appropriate for the infection?

These basic questions should be considered upon suspicion of infection and regularly throughout the course of antibiotic treatment. Often, antibiotic stewardship results in fewer days of antibiotic therapy and a narrower spectrum of coverage. On occasion, as driven by clinical course or availability of resistance information, stewardship leads to broadening of coverage and/or duration of treatment. The key is to "match the drug to the bug!"

**Secondary Driver > ADOPT AND ADAPT EVIDENCE-BASED GUIDELINES**

Guidelines exist matching antibiotics to specific infections, based on the bacteria suspected or identified or the source of infection.\(^{28, 29}\) It should be noted that these antibiotic treatment guidelines are in fact just that: guidelines. When coupled with local antibiotic resistance patterns, these guidelines can serve as a basis for the development of a specific organization’s guidelines.

**Change Ideas**

> Review national antibiotic treatment guidelines, and compare the information with local antibiograms.
> Based on this review, begin to develop local recommendations for antibiotic treatment based on bacteria and source of infection.
> Work with champions in various departments to review and test your draft antibiotic treatment recommendations.
> Start small with a narrow focus.

**Suggested Process Measures for Your Test of Change**

- Percent of key medical staff leaders who reach agreement on guidelines.
- Sample 20 patients, and report the number who received inappropriate orders.
- Number of patients who had asymptomatic bacteruria yet were treated with antibiotics for a ‘urinary tract infection’.

**Secondary Driver > STANDARDIZE TIMELY CULTURE & SENSITIVITY (C&S) REVIEW**

The importance of timely identification of both bacterial pathogens and their sensitivities to antibiotics cannot be overestimated. Obtaining cultures prior to treatment remains a high priority. Just as important is the implementation of a reliable process to ensure that all available C&S results are identified and acted upon promptly. Various organizations successfully perform these activities in different ways due to different culture and resources. One thing that they have in common is that they all have “one owner” responsible for notification to the provider of these results. Owners can be laboratory personnel, pharmacists, nurse practitioners, or physicians, but the process should be defined and followed regardless of day or time of C&S results availability.

**Change Ideas**

> Develop, test, and implement standard workflows using the electronic health record to alert pharmacists, nurses, and physicians when C&S results are available.
> Test and implement direct provider-to-provider communication processes for unexpected C&S results.
> Use the "48-hour antibiotic time out" procedure discussed below to review C&S results on all patients who have been on antibiotics for 48 to 72 hours.
Suggested Process Measures for Your Test of Change

- Percent of patients who receive appropriate cultures prior to administration of antibiotics.
- Percent of C&S results acknowledged by the provider in a timely manner.
- Percent of C&S results where appropriate antibiotic changes occurred due to the C&S results.

Secondary Driver > APPLY STEWARDSHIP TECHNIQUES

Many strategies can be used, alone or in combination, to effectively steward antibiotics. The Infectious Diseases Society of America has published guidelines regarding these strategies. The "strong" recommendations are summarized in Appendix III.

ASP strategies can be generally classified as front-end or back-end. Most successful ASPs use both approaches. All approaches are facilitated by requiring the prescribing clinician to document the indication for the antibiotic so that all caregivers and the ASP can view it.

Front-end strategies require restrictive preprescription authorization (PPA) for all clinicians except a select group. This approach allows for targeting specific antibiotics for specific indications based on the organization’s guidelines developed using national recommendations adjusted for local resistance patterns. While these approaches can successfully limit the use of high-cost antibiotics, they may also result in increased, and possibly inappropriate, use of non-restricted antibiotics.

Back-end approaches use postprescriptive review and feedback (PPRF). The steward reviews current antibiotic orders and provides prescribers with recommendations to continue, change, or discontinue orders based on the clinical and microbiological patient information. Studies show that this approach provides the opportunity for discussion, learning, and de-escalation (narrowing coverage, changing to oral route, or discontinuation). As a result, there is decreased antibiotic use, decreased number of new prescriptions, and increased clinical satisfaction.

Evidence shows that both front-end and back-end approaches are effective, either alone and together. Tamma et al. found that while both PPA and PPRF were effective, PPRF alone had more impact on antibiotic Days of Therapy (DOT) than PPA alone. The authors suggest that PPRF might be an early focus of the ASP, especially if resources are limited.

In addition, newer laboratory testing that provides real-time, rapid diagnostics, such as rapid pathogen identification (influenza and methicillin-resistant S. aureus) and biomarkers, can aid in improving the appropriateness of antibiotic use.

A summary table of all key strategies, along with pros and cons, can be found in Appendix IV.

Change Ideas

- Require documentation of diagnosis for any antibiotic orders.
- Establish a 48-hour time-out for all patients who have received antibiotics for 48 – 72 hours. Review with the physician to determine if the current antibiotic coverage is appropriate.
- Select an antibiotic whose resistance you want to protect, and trial either PPA or PPRF or both on one unit.
- Trial antibiotic order sets and algorithms on paper with physician champions, then expand to one unit.
- Explore the costs and benefits of rapid-testing methodologies.
Suggested Process Measures for Your Test of Change

- Percent of antibiotics ordered where diagnosis is documented for viewing by the multidisciplinary team.
- Percent of initial orders changed through PPA process.
- Percent of patients receiving a 48-hour time-out antibiotic time-out.
- Percent of pharmacist-physician discussions prompted by 48-hour time-outs that lead to de-escalation.
- Percent of antibiotic orders that are compliant with facility adopted guidelines.

Secondary Driver > KNOW WHEN AND HOW TO SAY “NO”

Studies report that two of the most common reasons that physicians prescribe antibiotics when those antibiotics are not indicated are because of social pressure from the patient or family member, or because of uncertainty or fear that they might be overlooking a bacterial infection. The “Choosing Wisely” campaign can serve as a valuable tool to remind physicians when antibiotics are not appropriate.40

Change Ideas

> Focus on the history and physical exam, not “How can I help you?”
> Narrate your findings aloud to reaffirm the lack of a bacterial infection.
> Lead with what will make the patient feel better, not that you are withholding antibiotics.
> Remind the patient that antibiotics can and do make patients sick, and that adverse events are not rare.
> Educate the patient that the patient might need antibiotics in the future, and that taking them unnecessarily now may make it harder to treat a future infection.
> Seek another opinion from a clinician or an antibiotic steward when you are not sure if a patient needs an antibiotic.

Suggested Process Measures for Your Test of Change

- Survey results of physicians regarding their comfort level and need for scripting to say "no."
- Percent of patients treated in the Emergency Department with antibiotics for sinusitis, pharyngitis, bronchitis, and asymptomatic bacteruria.
- Percent of patients identified during review who were prescribed antibiotics upon admission who did not meet criteria for antibiotics.

Hardwire the Process

Education and guidelines are important but insufficient to create a meaningful ASP. The ASP should be hardwired by implementation of either PPA or PPRF, supported by other strategies such as the 48-hour time-out, order sets and algorithms, or computer-assisted decision support.
Primary Driver:

**AIM, MEASURE, ANALYZE, AND REPORT**

All improvement activities benefit from setting an aim, performing tests of change, measuring and analyzing the results, and reporting them along with lessons learned to executive sponsors, leadership, and all engaged in the work.

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**Secondary Driver > DETERMINE AIMS**

Though there is no national specific aim for an ASP, research shows that ASPs are important to improving patient care. Since, as noted above, it is estimated that 30-50% of antibiotics administered in hospitals are not necessary or wrong in drug, dose, or duration, reduction is possible without reducing administration of necessary antibiotics.

**Change Ideas**

- Set aims based on obtainable metrics. DOT is preferred; if it is difficult to obtain, DDD is acceptable.
- Start small, with one unit or one class of antibiotics.
- Segment by unit, especially the ICU, as often the DOT or DDD are highest there, but can vary widely among units, specialties, and providers.
- Compare your organization’s antibiotic use with that of similar hospitals (Standardized Antibiotic Administration Ratio) by joining the CDC’s Antimicrobial Usage and Resistance program. Remember though that because average antibiotic usage is woefully high, having a SAAR of 1.0 means that the usage is average, leaving much room for improvement!

**Suggested Process Measures for Your Test of Change**

- Percent of DOT or DDD numerators and denominators validated by record review for one unit for one week.
- Percent of patients who have a urinalysis and urine culture obtained in the Emergency Department AND are prescribed antibiotics.

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**Secondary Driver > MONITOR AND REPORT REGULARLY**

Data collection alone does not create improvement. The measures decided upon should be reported and discussed at all meetings for nurses, pharmacists, physicians, and leadership, and posted appropriately in an easy-to-read manner. These discussions should provide feedback to guide new tests of change or to spread effective practices.

**Change Ideas**

- Start by reporting small tests of change to the ASP implementation team and its medical staff and executive sponsors.
- Measure and report associated data, such as adverse drug reactions to antibiotics.
- Report balancing measures to ensure the ASP is not causing harm through the withholding of necessary antibiotics or the minimization of histories of allergic reactions.
- If possible, create and report your organization’s antibiogram semi-annually or quarterly.

**Suggested Process Measures for Your Test of Change**

- Percent and frequency of meetings with each discipline and leadership where ASP measures are reported and discussed.
- Placement of ASP updates on the agenda: first, middle, or last.

**Hardwire the Process**

Create pharmacy reports to measure DOT, DDD, and/or SAAR, along with processes to identify any patients harmed by overreaching ASP strategies. Marry these data to rates of adverse drug reactions from antibiotics. Plot these on the same run chart for simultaneous visual reporting and interpretation. Create reports no less often than monthly, and as often as weekly where possible during your focused tests of change.
Primary Driver
ENGAGE PATIENTS AND FAMILIES

Patient expectations that antibiotics will help their illness appears to be a common driver of antibiotic overprescribing. Physicians can feel pressured to fulfill those expectations, and when pressured, can lose objectivity regarding the need for antibiotics. Engagement of patients and families can assist in reducing inappropriate prescribing.

Secondary Driver > USE MULTIPLE MODALITIES TO TEACH RISKS AND APPROPRIATENESS

Education regarding the risks of inappropriate use of antibiotics should be provided to patients and families. The Choosing Wisely campaign, The Joint Commission, and the CDC all offer several tools for patient education.

Change Ideas

> Share various educational tools with patients of different backgrounds and seek their reaction.
> Offer publications, videos, and website addresses to patients and families.
> Distribute educational materials online through the organization’s website.
> Promote Antibiotic Awareness Week.
> Discuss the pros and cons of antibiotics with patients, and learn their understanding of the potential for harm.
> Ask the patient if they have ever had any side effects from antibiotics. If so, reinforce their experiences.
> Relay stories of patients who suffered from *C. difficile* as a result of antibiotics.

Suggested Process Measures for Your Test of Change

- Survey patients’ reactions to various materials and modalities.
- Measure the impact of antibiotic stewardship education on patient demand as reported by physicians.

Secondary Driver > TEACH WHAT TO DO IF ANTIBIOTICS ARE ORDERED

Several patient-friendly resources exist to help patients refrain from seeking or taking antibiotics.

Change Ideas

> If antibiotics are ordered, the patient or family can ask the physician to explain why, specifically, each one is necessary.
> The patient or family can ask when the need for antibiotics will be reviewed.
> If the patient is still on antibiotics after three days, the patient or family can seek an understanding of why, and ask if the antibiotics can be narrowed in scope, reduced in duration, or discontinued.

Suggested Process Measures for Your Test of Change

- Percent of patients who ask why antibiotics are necessary.
- Percent of patients who report satisfactory understanding of need for the specific antibiotic received and the duration of treatment.

Hardwire the Process

Set expectations regarding antibiotic prescribing up front before the patient encounters the provider. At intake, offer brief education regarding inappropriate uses of antibiotics and the associated harm. Upon admission, use simple verbal and written information to educate patients and families to ask why antibiotics are necessary and to ask when the need for them will be reviewed.
Choice of Tests and Interventions for Antibiotic Stewardship: There are many potentially effective interventions to improve antibiotic stewardship. Improvement teams should begin their efforts by asking: “What is our current level of stewardship? What’s working? What’s not? What should be our next steps?”

Here are some suggestions:

1. Assemble a multi-disciplinary team, and thoughtfully perform the gap analysis.

2. Have pharmacists discuss with champion physicians every patient who has been on antibiotics for 48 hours or more to help determine necessity, scope, and duration of therapy.

3. Focus on high-risk positive cultures, such as blood, or cultures often ordered, such as urine cultures, and review data to determine the most commonly prescribed broad-spectrum antibiotics; then review ten charts of patients on these antibiotics to assess appropriateness.

4. Review C&S data at 48 hours on the next ten patients receiving antibiotics, and compare results with scope of coverage.

5. Consider the role of all leaders and caregivers: where can each contribute?

### IMPLEMENT SMALL TESTS OF CHANGE

#### Test the 48-Hour Antibiotic Time-Out

<table>
<thead>
<tr>
<th>PLAN</th>
<th>Identify a pharmacist champion to contact the physician of each patient who has received inpatient antibiotics for 48 – 72 hours.</th>
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<tr>
<td>DO</td>
<td>For a week (or one day if volume is high), the pharmacist will review the chart and the culture and sensitivity (C&amp;S) results of each of these patients and then call the physician to discuss the patient’s current status and to attempt to answer these key questions:</td>
</tr>
<tr>
<td></td>
<td>&gt; Does the patient have an infection?</td>
</tr>
<tr>
<td></td>
<td>&gt; If the patient has an infection, is it a bacterial infection?</td>
</tr>
<tr>
<td></td>
<td>&gt; If it is a bacterial infection, what is the likely source?</td>
</tr>
<tr>
<td></td>
<td>&gt; If it is a bacterial infection, is C&amp;S information available?</td>
</tr>
<tr>
<td></td>
<td>&gt; If C&amp;S information is not available, based on the patient’s history or the local antibiogram, is the bacteria likely to be resistant to usual treatment?</td>
</tr>
<tr>
<td></td>
<td>&gt; Is the duration of therapy appropriate for the infection?</td>
</tr>
<tr>
<td>STUDY</td>
<td>Assess and record the physicians’ reaction (qualitative) and the results of the interaction (antibiotic changed, discontinued, or change in duration or dose).</td>
</tr>
<tr>
<td>ACT</td>
<td>Review results, then plan a new test of change to improve reactions and results. Consider adding a second pharmacist to the test of change.</td>
</tr>
</tbody>
</table>
Potential Barriers

> Many potential barriers to the development of an effective ASP exist. Common barriers include physician resistance to non-physician “meddling” in the care of their patients; lack of organizational ASP knowledge and capacity; lack of clarity regarding roles and responsibilities, and lack of protected time and resources required for ASP development and success. In addition, pushing an ASP as primarily a *money-saver will likely disengage clinicians.*

Enlist Administrative Leadership as Sponsors to Help Remove or Mitigate Barriers

> As discussed in relation to the first driver, Create Organizational Will, leadership is key to overcoming the barriers identified above. Effective and honest communication, transparency of data and purpose, engagement of champions, starting small in scope and segmentation, and the provision of needed training, time, and resources are all domains in which leadership can create the opportunity for success.

Change not only “The Practice,” but also “The Culture”

> Moving from a process where physicians autonomously order antibiotics to one of physician-pharmacist collaboration regarding antibiotics requires culture change. A key to promoting this change is for the pharmacist to exhibit his or her knowledge of antibiotics and then engage the physician as a partner and resource, rather appearing to question or second-guess the physician’s antibiotic orders. Working together to *protect antibiotics is likely to promote collegial care better than working to restrict antibiotics.*

**PART 4: CONCLUSION AND ACTION PLANNING**

Effective antibiotic stewardship is overdue. Each organization has a duty to provide patients with optimal care. Antibiotic stewardship is fully aligned with the Triple Aim of healthcare: “improving the patient experience of care (including quality and satisfaction), improving the health of populations, and reducing the per capita cost of health care.”

The suggested next step: Perform your gap analysis, found here: 
PART 5: CASE STUDIES

ANTIBIOTIC STEWARDSHIP PROGRAM (ASP) CASE STUDY: LARGE MEDICAL CENTER

Mississippi Baptist Medical Center

Location: Jackson, Mississippi
Bed Size: 541

Key Contact (name/email):
Tripp Dixon  tdixon@mbhs.org

Duration of organized ASP: Since 2011

Organization and governance of ASP:

> Leader or co-leaders (names, roles):
  - Tripp Dixon, PharmD
  - Mike Byers, MD,
    Infectious Disease Specialist

> Members of task force or committee (no names, just roles):
  - Pharmacists:
    - Tripp Dixon, PharmD,
      Clinical Pharmacy Specialist
    - Matt Chambers, PharmD
      Clinical Pharmacy Specialist
    - Phil Ayers, PharmD
      Chief, Clinical Pharmacy Services
  - Clinical Microbiologist:
    - Gloria Luckett
  - Infection Control Coordinators:
    - Susan Taylor, MS, MT, SM, CIC
    - Erica Payne, RN
  - Information Systems Specialist:
    - Jerry Smith, RPh
      Pharmacy Applications Manager
    - Baron Matthews
      Interface Specialist

> Governance:
  - Meets quarterly
  - Reports to P&T quarterly, which filters to medical executives and the board
  - Updates to quality, infection prevention, and surgical committees

List all strategies of ASP implemented with key details:

Broad Interventions

a. Limited antibiotic restriction to specific indication(s) and specialty
b. Seven day limit on antibiotics ordered without a specified stop date
c. Annual antibiotic susceptibility panel review
d. Antibiotic review occurs on daily interprofessional rounds
e. Daily antibiotic surveillance alerts available for review:
   i. De-escalation opportunities
   ii. Duplicate antibiotic coverage alerts
   iii. Antimicrobial — antibiotic mismatch reports
   iv. Antimicrobial usage audits
Pharmacy-Driven Interventions
  a. Automatic intravenous to oral antibiotic policy
  b. Automatic renal dose adjustment policy
  c. Prospective audit and feedback of organism and antibiotic mismatches and duplications

Diagnosis and Infection Specific Interventions
  a. Disease Specific Orders Sets
     i. Healthcare Associated Pneumonia
     ii. Community Acquired Pneumonia
     iii. Sepsis
     iv. Neutropenic Patients

Stewardship Metrics
  a. Infection Control
     i. Healthcare associated infections
        1. Central line associated infections
        2. Catheter associated infections
     ii. C. difficile rates
  b. Antibiotic use: Days of Therapy/1000 patient days
  c. Annual Antibiogram

Reporting
  a. Antibiogram is published on the intranet and is accessible to all staff
  b. Metrics being tracked are shared with relevant staff and committees
  c. Direct, personalized communication with specific prescribers occurs when appropriate

Patient Education
  a. Indications for and adverse effects of antibiotics are explained to the patient and, when appropriate, family members
  b. The Center for Disease Control and Prevention’s Get Smart document, Viruses or Bacteria — What’s got you sick? is posted in common areas and distributed to patients and families on admission
  c. Patients and relevant family members are educated on isolation precautions as needed

Staff and Prescriber Education
  a. Antimicrobial Stewardship centered lectures routinely made available to prescribers
  b. Antibiotic initiatives and facility specific metrics are communicated via internal electronic and print media when appropriate
  c. Direct, personalized education with specific prescribers occurs when appropriate

TIMELINE FOR IMPLEMENTATION:

Formulary restriction and the production of an annual antibiogram have been in place for several years. The formal Antimicrobial Stewardship Team, initiated in 2011, took ownership of reviewing current restrictions, antimicrobial containing order sets, the annual antibiogram, susceptibility panels and a variety of other initiatives. These are updated on an ongoing basis (i.e. as new antimicrobials are added to formulary and new evidence based medicine is published).
In the first three years and in addition to the above activities, automatic IV to PO protocol, renal dose adjustment protocol, requirements for antimicrobial reordering, and a software surveillance system were implemented.

In the last three years, daily rounds throughout the hospital were started and antibiotic review was incorporated into those rounds. The primary metric of DOT/1000 patient days was chosen to evaluate antimicrobial use and is shared in presentations to appropriate committees and prescribing staff.

**Barriers and Strategies Employed to Overcome Barriers:**

**Prescriber Resistance to Automatic Protocols and Antimicrobial Reordering Policy**

This was overcome by using best practices from other sites, meeting with various individual prescribers and physician groups to garner buy-in and having the support of hospital administration and a respected ID physician champion.

**Investment in Resources**

Literature was gathered to identify the economic benefits and importance of a formal antimicrobial stewardship program. This information was used to obtain the support of pharmacy and wider hospital leadership, to designate a pharmacy and physician leader and to purchase software surveillance and other resources to improve anti-infective use.

**Time**

Antimicrobial surveillance software was used to identify opportunities. Protocols approved by the prescribing staff and governing hospital committees were implemented to allow for the automatic adjustment of antimicrobials based on pre-specified criteria.

**Prescriber and Patient Education**

A variety of electronic media, physical posters and place cards were used in prescriber and patient specific areas and at lecture series and prescriber events.

**Results:**

- Current data from 2017 projects to show a 7-10% reduction in targeted antimicrobial use.

- Complete data from 2015 to 2016 show:
  - Overall reduction in targeted antimicrobial use (including, but not limited to):
    - 5% reduction of carbapenem use
    - 16% reduction of daptomycin use
    - 55% reduction of tigecycline use

**Next steps:**

- Continue to add infectious disease related pathways and order sets

- Develop enhanced system for providing individualized feedback to prescribers regarding anti-infective use

- Focus efforts on innovating creative ways to educate prescribers and patients on the appropriate use of antibiotics
ANTIBIOTIC STEWARDSHIP PROGRAM (ASP) CASE STUDY: CRITICAL ACCESS HOSPITAL

Southwest Health System

Location: Cortez, Colorado
Bed Size: 25

Key Contact (name/email): Marc Meyer mmeyer@swhealth.org

Duration of organized ASP: Since October 2014

Organization and governance of ASP:

- Leader or co-leaders (names, roles):
  - Marc Meyer Pharmacist, Infection Preventionist
- Members of task force or committee (no names, just roles):
  - Hospitalist
  - ED physician
  - Wound care specialist, PT
  - RN Educator
  - RN ICU
  - RN medical clinics, oversees all clinics
  - Pharmacists
  - Lab microbiologist
  - Physician Assistant form clinics
  - Nurse Practitioner form clinics
- Governance:
  - Meets quarterly
  - Reports to P&T quarterly, which filters to medical executives and the board
  - Updates to quality, infection prevention, and surgical committees

List all strategies of ASP implemented with key details:

1. Formal stewardship support
2. Financial support (part of pharmacy budget)
3. Accountability falls on the pharmacists, but there is also a physician leader
4. Drug expertise is provided by the pharmacy
5. Our team is wide and varied
6. We have a stewardship policy
7. We have daily rounds where 48 time out and de-escalation occur
8. We have nine antimicrobials that are restricted that need to be approved by pharmacy
9. Audit and feedback is performed
10. There are no automatic changes from IV to po; those are discussed in daily rounds
11. Dose optimization occurs on all orders at order approval by pharmacy
12. Time-sensitive stop orders are input into the system on almost all antimicrobials orders
13. We have specific interventions for UTI, SSI, Community Acquired Pneumonia, surgical prophylaxis, MRSA empiric treatment, CDI and culture proven blood stream infections

14. We report to the Antibiotic Use (AU) of the CDC (click here for more information) and use an affordable software vendor to look at data (driven down to prescriber level) and to monitor specific interventions

15. We track *C. difficile* rates and monitor problem pathogen histories in our system

16. We produce a yearly antibiogram

17. We monitor the Days of Therapy (DOT)/1000 patient days via the AU module and Asolva Medici AU

18. We are processing a way to share provider specific reports for our hospital and clinic staff

19. We have had three education sessions on stewardship for national experts in the last 12 months and we provide ongoing stewardship education locally for staff, medical staff, dentists, nursing homes and clinics

20. We have a clinic stewardship project for UTI and URI for both adults and peds

21. We have a Long Term Care project in a local nursing chain for 500 beds for UTI

---

**Key milestones:**

> In October 2014 we became part of the Colorado Hospital Association Collaborative leadership and adopted the statewide UTI and SSTI project in our hospital.

> In December 2015, we participated in the NQF project that authored a playbook for hospital stewardship that came out in May 2016.

> In July 2016, Marc Meyer gave a webinar with Arjun Srinivasan, MD, Associate Director for Healthcare-Associated Infection Prevention Programs at the CDC, titled Stewardship in a Limited Resource Setting, available here.

> In April 2017, CDC and Pew convened a group of CAH content experts that included Marc Meyer from Southwest Health System to write a CAH stewardship guide. The guide was published in July and is available here.

> In May 2017, Marc Meyer co-authored a paper in Clinical Infectious Diseases on problems with stewardship in small hospitals, available here.

> In July 2017, Marc Meyer was invited by the CDC to post a Safe Healthcare blog, Antibiotic Stewardship in Action: Southwest Health System’s Approach. This launched the release of the CAH guide above. It is available here.

> In July 2017, the SHS stewardship program was featured in a report by the CDC, Antibiotic Use in the United States: Progress and Opportunities, available here.

> Throughout 2017, Marc Meyer of Southwest Health System has served as a teacher and consultant to the CDC, Oregon, Washington, South Dakota, Illinois, and Iowa.
TIMELINE FOR IMPLEMENTATION:

We have done stewardship in some form for the last 27 years: closed formulary, stop orders, antibiotic order sheets, surgical guidance, etc.

We developed an official team in late 2014 and it has become very robust, with programs in all areas of our small health system.

Barriers and Strategies Employed to Overcome Barriers:

**Good Data Collection.**
We converted old guard antibiotic usage ideology to new data drive and guidance drive usage among both new and old providers. Overcoming this barrier was difficult. We needed the Antibiotic Use module data and an easy way to upload it. We solved this with Medici Au, an Asolva product. It costs $50 per month for our 25 beds. It pulls MAR, transfer, admission and discharge data from our system to the cloud, where it uploads to the AU module in NHSN and also give us the ability to look at our antibiotic usage from as high as 30,000 feet right down to level of a single provider.

**Time!**
Solving the data collection barrier also went a long way towards solving the time barrier. Not only was much time saved in obtaining data, but good data lessened the time for adoption.

Results:

> Total antibiotic use is < 1/3 less than the NHSN AU mean for CAHs
> Levofloxacin use decreased 40%
> Additional problem areas that the data has helped us identify include:
  • Periodic increases in vancomycin use
  • Higher than mean SAAR for MDRO antibiotics on our medical surgical department

Next Steps:

> Become more robust using NHSN AU data to analyze our problem areas in combination with Asolva Medici AU.
> Dive into antibiotic use patient by patient in those areas in retrospective review.
> Work with our outpatient sites to improve antibiotic use
> Work with local dentists and veterinarians to assist them with stewardship issues.
> Measure the effect of community stewardship on MDRO’s reported by our lab (which provides service to a 2-county area).
> Work with our wound expert to develop a wound guide for the system.
PART 6: APPENDIX

APPENDIX I: TOP TEN CHECKLIST

Associated Hospital/Organization: AHA/HRET HIIN

Purpose of Tool: The Top Ten Checklist is provided to support your facility’s understanding of where there are opportunities to address this harm or sustainability efforts that may need attention.

Reference: AHA/HRET HIIN Antibiotic Stewardship Change Package

<table>
<thead>
<tr>
<th>2017 Antibiotic Stewardship Top Ten Checklist</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Focus on <em>protecting, not restricting key antibiotics</em></td>
</tr>
<tr>
<td>2. Focus on improving patient care, not on saving money; effective stewardship will save money</td>
</tr>
<tr>
<td>3. Secure leadership commitment</td>
</tr>
<tr>
<td>4. Perform gap analysis</td>
</tr>
<tr>
<td>5. Establish program governance, including roles and responsibilities</td>
</tr>
<tr>
<td>6. Effectively communicate with leaders, managers, providers, pharmacists, nurses, and patients and families</td>
</tr>
<tr>
<td>7. Provide ASP training for ASP leaders</td>
</tr>
<tr>
<td>8. Know the current state: collect and review current antibiotic usage data</td>
</tr>
<tr>
<td>9. Review and develop a plan for implementation of selected antibiotic stewardship techniques</td>
</tr>
<tr>
<td>10. Measure and report regularly with transparency and visibility</td>
</tr>
</tbody>
</table>
Summary of Core Elements of Hospitals Antibiotic Stewardship Programs

Leadership Commitment > Dedicating necessary human, financial, and information technology resources.

Accountability > Appointing a single leader responsible for program outcomes. Experience with successful programs shows that a physician leader is effective.

Drug Expertise > Appointing a single pharmacist leader responsible for working to improve antibiotic use.

Action > Implementing at least one recommended action, such as systemic evaluation of ongoing treatment need after a set period of initial treatment (i.e., “antibiotic time-out” after 48 hours).

Tracking > Monitoring antibiotic prescribing and resistance patterns.

Reporting > Regular reporting information on antibiotic use and resistance to doctors, nurses, and relevant staff.

Education > Educating clinicians about resistance and optimal prescribing.
Summary of IDSA “Strong” Recommendations for Antibiotic Stewardship Program Implementation

RECOMMENDATION

> Use Preauthorization and/or prospective audit and feedback over no such interventions.

> Use antibiotic stewardship interventions designed to reduce the use of antibiotics associated with a high risk of C. difficile infection compared with no such intervention.

> Implementation of pharmacokinetic monitoring and adjustment programs for aminoglycosides.

> Implementation of interventions to increase the use of oral antibiotics for initial therapy and the timely transition of patients from IV to oral antibiotics.

> Implementation of guidelines and strategies to reduce antibiotic therapy to the shortest effective duration.
## APPENDIX IV: SUMMARY OF KEY ASP STRATEGIES

**Associated Hospital/Organization:** HRET/HIIN

**Purpose of Tool:** List of key strategies for implementing an Antibiotic Stewardship Program.


### SUMMARY OF KEY ASP STRATEGIES

<table>
<thead>
<tr>
<th>STRATEGY</th>
<th>PROS</th>
<th>CONS</th>
</tr>
</thead>
</table>
| **PREPRESCRIPTION AUTHORIZATION (PPA)** | > Limits access to selected antibiotics | > Can increase the use of other antibiotics and may not decrease total use.  
> Requires authorization pathway, including consideration of the need for after-hours authorization. |
| **Postprescriptive Review and Feedback (PPRF)** | > Encourages communication and discussion, and creates learning loops.  
> Can reduce targeted antibiotics as well as all antibiotic use.  
> More likely to be accepted by prescribers. | > Initial inappropriate use of targeted antibiotics is not prevented. |
| **48-HOUR TIME-OUT**        | > Prompts multidisciplinary discussion of appropriateness of current antibiotic orders, and often leads to de-escalation (narrower spectrum, shorter duration, or discontinuation). | > Potential physician resistance, but generally easily overcome as physician experiences value of pharmacist’s assistance. |
| **FORMULARY RESTRICTION**   | > Reduces antibiotic choice to manageable number, reduces duplicate therapy, decreases costs. | > May be a challenge for hospitals with providers or specialists who work in many hospitals and find it difficult to use different formularies at each. |
| **ORDER SETS AND TREATMENT ALGORITHMS** | > Prompts the prescriber to make choices based on likely bacteria or source of infection, consider allergies, adjust for renal function, consider cost, and order appropriate tests and consultations.  
> Allows for default algorithmic orders for common conditions for drug, dose, and duration.  
> Can be paper or electronic. | > Must allow for opt out with explanation. |
## SUMMARY OF KEY ASP STRATEGIES

<table>
<thead>
<tr>
<th>STRATEGY</th>
<th>PROS</th>
<th>CONS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CLINICAL GUIDELINES</strong></td>
<td>&gt; Provides the opportunity to include many leaders to develop hospital-specific guidelines and algorithms.</td>
<td>&gt; Important and effective when coupled with PPA or PPRF. Lesser effectiveness as stand-alone strategy.</td>
</tr>
<tr>
<td></td>
<td>&gt; Allows for communication to frontline caregivers who are not infectious disease specialists.</td>
<td>&gt; Note: Infectious disease specialists are not required for guideline development. Any physician and/or pharmacist champion may lead this effort.</td>
</tr>
<tr>
<td><strong>EDUCATION</strong></td>
<td>&gt; Necessary for buy-in and discussion and use of order sets, algorithms, and guidelines.</td>
<td>&gt; Required but not sufficient as a stand-alone strategy.</td>
</tr>
<tr>
<td><strong>PHARMACODYNAMIC DOSE OPTIMIZATION</strong></td>
<td>&gt; Using a pharmacodynamics parameter correlated with efficacy, PK Monitoring optimizes bacterial killing and decreases the emergence of resistance.</td>
<td>&gt; Cost.</td>
</tr>
<tr>
<td>(PK MONITORING)</td>
<td>&gt; This strategy has been applied to beta-lactams, ciprofloxacin, vancomycin, and cefepime.</td>
<td></td>
</tr>
<tr>
<td><strong>COMPUTER ASSISTED DECISION SUPPORT</strong></td>
<td>&gt; Provides real-time guidance and feedback to prescribers, and the option to monitor prescribing practices and create prior authorization mechanisms.</td>
<td>&gt; None</td>
</tr>
<tr>
<td>PROGRAMS</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>PHARMACIST-DRIVEN INTRAVENOUS TO ORAL</strong></td>
<td>&gt; Pharmacists have heightened awareness of the oral bioavailability of antibiotics, and can initiate timely IV to oral administration for patients who meet criteria. Drugs often suitable for early IV to oral conversion include fluoroquinolones, metronidazole, macrolides, doxycycline, clindamycin, and linezolid.</td>
<td>&gt; Potential medical staff resistance to pharmacist orders.</td>
</tr>
<tr>
<td><strong>PHARMACY DOSING PROGRAMS</strong></td>
<td>&gt; Pharmacist-managed dosing for vancomycin and aminoglycosides has been shown to reduce mortality, length of stay, adverse events, and costs.</td>
<td>&gt; Clinicians, particularly residents, will lose or fail to learn dosing skills because of exclusion from the dosing and learning loop.</td>
</tr>
</tbody>
</table>
REFERENCES


