Antibiotic and Lab Stewardship to Prevent *Clostridioides difficile* Infections (CDI)

CENTERS FOR DISEASE CONTROL AND PREVENTION

HRET
HEALTH RESEARCH & EDUCATIONAL TRUST

STRIVE
States Targeting Reduction in Infections via Engagement

Presenter

Jeff Rohde, MD

Clinical Associate Professor of Internal Medicine
University of Michigan

Contributions by

Erik Dubberke, MD, MPSH
Washington University School of Medicine

Linda Greene, RN, MPS, CIC, FAPIC
University of Rochester, Highland Hospital

Karen Jones, RN, MPH, CIC
University of Michigan

Learning Objectives

- Explain the mechanisms by which antibiotic stewardship impacts *C. difficile* infections

- Describe examples of how implementing core elements of antibiotic stewardship impacts *C. difficile* infections

- Outline the role of diagnostic testing stewardship in preventing *C. difficile* infections
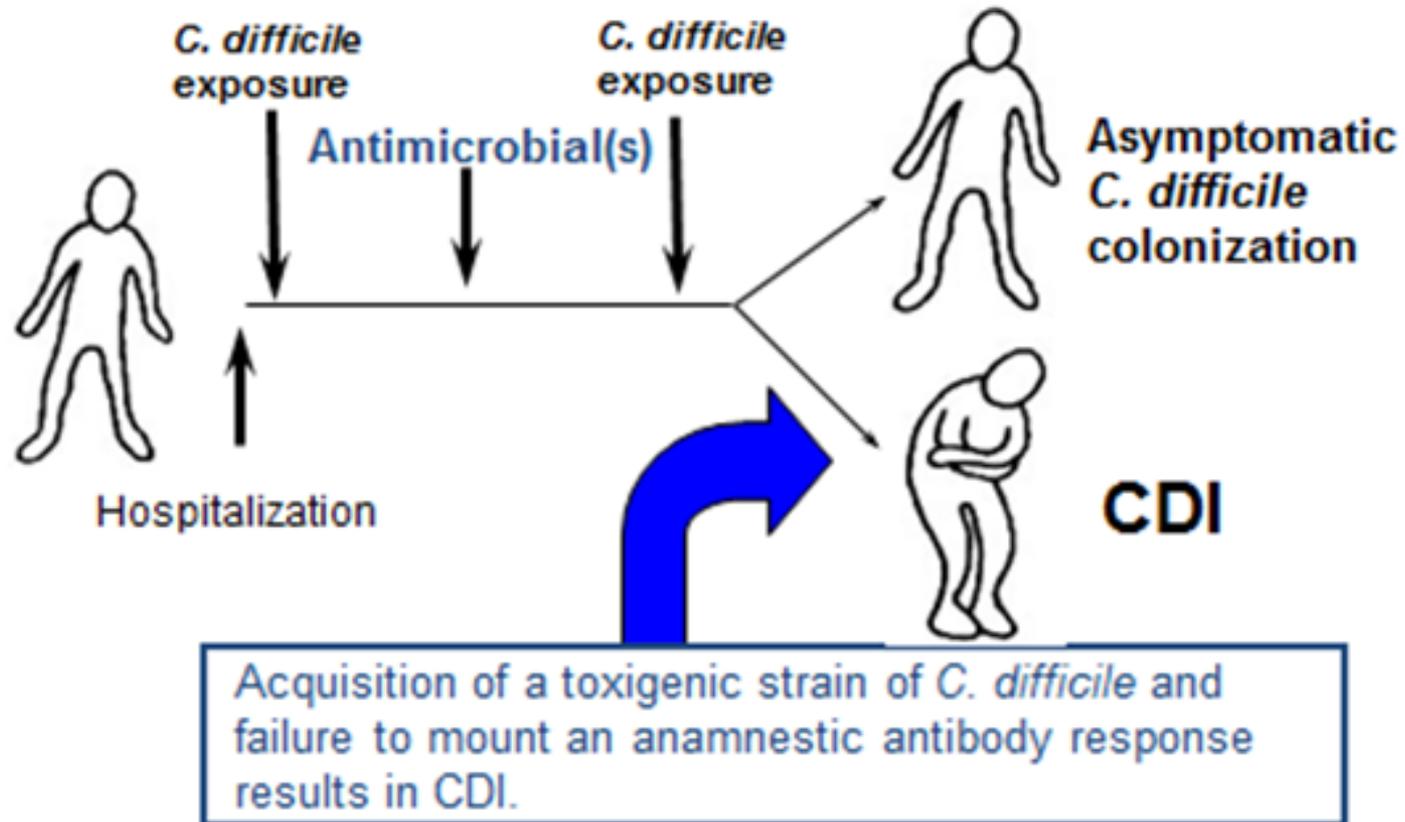
Antibiotic Use is Common in Acute Care

- Survey of 11,282 patients in 183 United States hospitals found that 50% of patients were being treated with at least one antibiotic

- Exposure to antibiotics is the single most important risk factor for *C. difficile* infection (CDI)
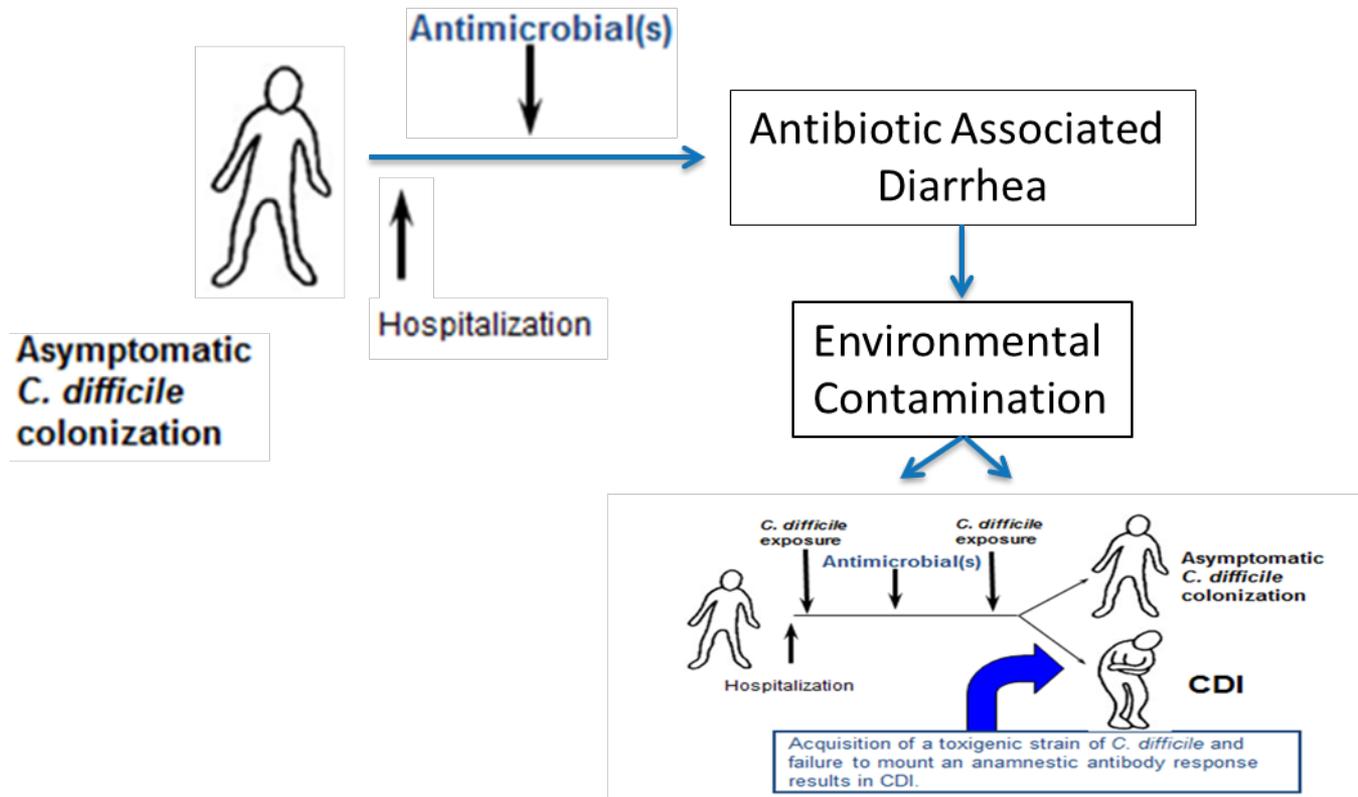
(Magill SS, JAMA, 2011; Get Smart Program, CDC)

Antibiotic Stewardship's Impact on CDI in Individuals

(Johnson S, Gerding DN. Clostridium difficile –associated diarrhea.
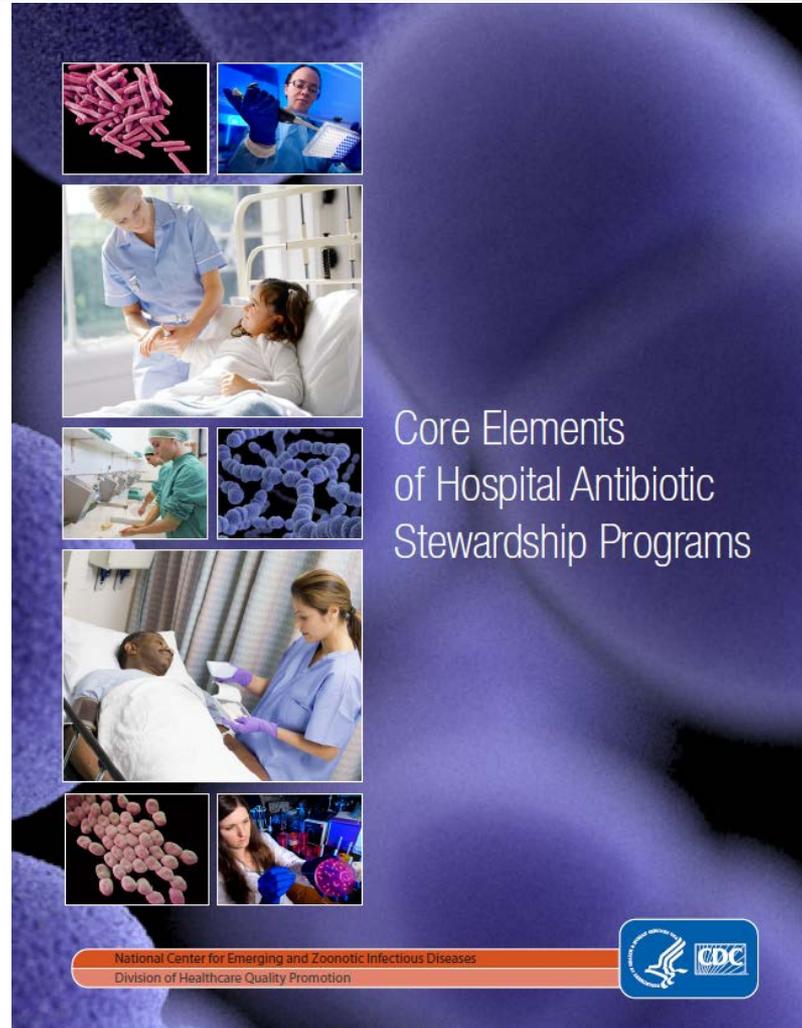*Clin Infect Dis. 1998; 26(5):1027–1034. - Kyne. NEJM 2000)*

Antibiotic Stewardship's Impact on CDI in a Ward or Hospital

(Johnson S, Gerding DN. Clostridium difficile –associated diarrhea. Clin Infect Dis. 1998; 26(5):1027–1034. - Kyne. NEJM 2000)

CDC's Core Elements of Antibiotic Stewardship for Acute Care Hospitals

(Core Elements of Hospital Antibiotic Stewardship Programs, CDC, 2014)

Core Elements of Hospital Antibiotic Stewardship Programs

1. **Leadership Commitment**: Dedicate resources

2. **Accountability**: Appoint a leader responsible for implementation

3. **Drug Expertise**: Appoint a pharmacist leader

4. **Actions to Improve Use**: Implement at least one recommended action

5. **Tracking**: Monitor antibiotic prescribing and resistance patterns

6. **Reporting**: Regularly report on antibiotic use and resistance

7. **Education**: Train staff, patients and families about resistance and optimal prescribing

(Core Elements of Hospital Antibiotic Stewardship Programs, CDC, 2014)

Leadership Commitment

- Leadership support is critical for success
  - It can take many forms

- Antibiotic stewardship programs that focus on CDI pay for themselves through savings
  - Antibiotic costs
  - Indirect costs
    - Additional 12 hospital days
    - Increase of $29,000 in cost

(Lipp MJ, J Gastroenterol Hepatol, 2012)

Drug Expertise and Accountability

- Identify a physician leader responsible for antibiotic stewardship outcomes
  - Infectious diseases physician
  - Hospitalist
  - Part-time/off-site

- Identify a pharmacy leader to co-lead antibiotic stewardship programs

(Srinivasan A, J Hosp Med, 2011)

Action: Intervention Categories

Broad

- Institutional policies/guidelines

- Formal review "antibiotic time-out"

- Restricted or pre-authorization of specific antimicrobials

- Prospective physician or pharmacist review with feedback

Pharmacy/Lab-Driven

- IV to PO conversion protocol

- Dose adjustments for organ failure

- Alerts for duplicative therapy

- Time sensitive automatic stop orders

Infection Specific

- Interventions to ensure optimal use of antibiotics for common infections:

  - CAP

  - UTI vs ABU

  - Skin/soft tissue

Antibiotic Stewardship Impact on CDI in One Hospital

- **Setting**: 4 medical wards in a community hospital in Canada with 1.85 cases of HA-CDI per month

- **Targeted antibiotic(s)**:
  - Fluroquinolone or second generation cephalosporin
  - IV for > 48hrs
  - Duration for > 5 days

- **Action:** Prospective audit and feedback by infectious diseases physician and pharmacist to the primary team

- Overall reduction in HA-CDI of 52%

(DiDiodato G, PLoS ONE, 2016)

Antibiotic Stewardship's Impact on High Risk Prescribing

- **Setting**: large community hospital in Toronto with 2 hospital-wide CDI outbreaks

- **Targeted antibiotic(s)**: ciprofloxacin

- **Action**: Not reporting Enterobacter sensitivity to ciprofloxacin when there was sensitivity to other agents (e.g. trimethoprim/sulfamethoxazole)

- Overall 55% reduction of ciprofloxacin use

(Langford BJ, J Clin Microbiol, 2016)

Case Study: Appropriate Antibiotics

- Ms. Anderson is a 68-year-old woman

- Has diabetes and hypertension

- Admitted to the hospital with a fever, productive cough and new 2L nasal cannula oxygen requirement

- Diagnosed with community-acquired pneumonia

What is the best antibiotic regimen to treat Ms. Anderson?

Disclaimer: All case studies are hypothetical and not based on any actual patient information. Any similarity between a case study and actual patient experience is purely coincidental.

Ms. Anderson's Case

- 2007 IDSA/ATS guidelines:
  - Respiratory fluoroquinolone or
  - Beta-lactam (preferred cefotaxime, ceftriaxone or ampicillin plus a macrolide)

- The patient is started on Ceftriaxone or Azithromycin for five days

- Overnight she clinically improves
  - Decreased fever
  - Decreased oxygen requirement

Disclaimer: All case studies are hypothetical and not based on any actual patient information. Any similarity between a case study and actual patient experience is purely coincidental.

Partner Actions to Improve Antibiotic Use and Reduce CDI

- Antibiotic time-out with the clinical pharmacist

- Institutional guidelines for antibiotic use for certain infections

Empiric Treatment of CAP in Non-ICU Patients

Preferred and Alternative Antibiotic Recommendations	
Preferred first-line therapy, for patients without penicillin allergy or risk factors for enteric GNR pneumonia*	Ampicillin-sulbactam 3gm IV q6 hr PLUS Azithromycin 500mg IV/PO x 1 day, then 250mg q24 hr x 4 days€

Ms. Anderson's Case Continued: Appropriate Testing

- Ms. Anderson is a 68-year-old woman

- Has diabetes and hypertension

- Recently treated for pneumonia with 14 days of levofloxacin

- During follow-up appointment complains of abdominal pain

Should Ms. Anderson be tested for *C. difficile*?

Disclaimer: All case studies are hypothetical and not based on any actual patient information. Any similarity between a case study and actual patient experience is purely coincidental.

CDI is a clinical diagnosis

Rates of Colonization with *C. Diff*:

- 3 to 7% of healthy adults

- 4 to 15% of hospitalized adults

- up to 50% of long-term care adults

(Dubberke ER, JAMA Intern Med, 2015)

Stool Threshold for *C. difficile* Testing

Bristol Stool Chart

Type 1		Separate hard lumps, like nuts (hard to pass)
Type 2		Sausage-shaped but lumpy
Type 3		Like a sausage but with cracks on its surface
Type 4		Like a sausage or snake, smooth and soft
Type 5		Soft blobs with clear-cut edges (passed easily)
Type 6		Fluffy pieces with ragged edges, a mushy stool
Type 7		Watery, no solid pieces. **Entirely Liquid**

(Caroffa DA, J Clin Microbiol, 2014)

19

Key Points About *C. difficile* Tests

- There is no "best" test to diagnose CDI

- Different facilities use different tests

Test	Specificity	Sensitivity
Antigen EIA	Lower	Higher
Toxin EIA	Higher	Lower
PCR	High	High
Culture/Cytotoxin assay	High	High

(Polage CR, JAMA Intern Med, 2015; Solomon DA, Open Forum ID, 2014)

Early Testing of *C. difficile*

- The longer it takes to identify CDI, the greater the chance for environmental contamination and potential transmission

- Keys:
  - Early identification of patients appropriate for testing
  - Early isolation
  - Early notification of test results

Back to Ms. Anderson's Case

- 68-year-old female

- s/p sub-optimal CAP treatment with abdominal pain

- We need more information

- Specifically, is she having loose stools or does she have an ileus?

Disclaimer: All case studies are hypothetical and not based on any actual patient information. Any similarity between a case study and actual patient experience is purely coincidental.

Potential Barriers and Countermeasures

Barrier	Countermeasure

• Discontinuity of care and handoffs;
   • Providers
   • Areas of care (unit, facilities, etc.)
	• Systemic automatic alert notifying current healthcare personnel and infection prevention department of positive result

• Resistance among providers to change practice
   • Isolation practices
   • Selectivity of testing
	• Measurement, reporting and education in a timely fashion
	• Multidisciplinary team (nursing, providers, lab, pharmacists)

Summary

- Focused antibiotic stewardship interventions can prevent *C. difficile* infections in a variety of ways

- *C. difficile* infection is a clinical diagnosis and there is no one best diagnostic test

- Early and targeted testing for *C. difficile* infection is crucial

References

- Biswas JS, Patel A, Otter JA, van Kleef E, Goldenberg SD. Contamination of the Hospital Environment From Potential Clostridium difficile Excretors Without Active Infection. *Infect Control Hosp Epidemiol.* 2015; 36: 975–7.

- Caroff DA, Edelstein PH, Hamilton K, Pegues DA. The Bristol stool scale and its relationship to Clostridium difficile infection. *J of Clin Microbio*l. 2014; 52(9): 3437–39.

- Core Elements of Hospital Antibiotic Stewardship Programs. US Department of Health and Human Services, CDC. 2014. Available at http://www.cdc.gov/getsmart/healthcare/pdfs/core-elements.pdf

- DiDiodato G, McArthur L. Evaluating the Effectiveness of Antimicrobial Stewardship Program on Reducing the Incidence Rate of Healthcare-Associated Clostridium Difficile Infection: A Non-Randomized Stepped Wedge, Single-Site, Observational Study. *PLoS ONE*. 11(6):e0157671.

- Dubberke ER, Burnham C-AD. Diagnosis of *Clostridium difficile* infection. JAMA Internal Medicine. 2015; 175(11):1801.

- Feazel LM, Malhotra A, Perencevich EN, Kaboli P, Diekema DJ, Schweizer ML. Effect of antibiotic stewardship programmes on *Clostridium difficile* incidence: A systematic review and meta-analysis. *J of Antimicrob Chemother*. 2014; 69(7):1748–1754.

- Get Smart Healthcare. Centers for Disease Control and Prevention, CDC. Accessed September 30, 2016, Available at http://www.cdc.gov/getsmart/healthcare/index.html

- Johnson S, Gerding DN. Clostridium difficile –associated diarrhea. Clin Infect Dis. 1998; 26(5):1027–1034. - Kyne. NEJM 2000.

References (Continued)

- Kyne L, Warny M, Qamar A, Kelly CP. Asymptomatic carriage of Clostridium difficile and serum levels of IgG antibody against toxin A. *N Engl J Med.* 2000; 342(6):390–397.

- Langford BJ, Seah J, Chan A, Downing M, Johnstone J, Matukas LM. Antimicrobial Stewardship in the Microbiology Laboratory: Impact of Selective Susceptibility Reporting on Ciprofloxacin Utilization and Susceptibility of Gram-Negative Isolates to Ciprofloxacin in a Hospital Setting. *J Clin Microbiol*. 2016; 54(9):2343-7.

- Lipp MJ, Nero DC, Callahan MA. Impact of hospital-acquired Clostridium difficile. *J Gastroenterol Hepatol*. 2012; 27(11):1733–7.

- Magill SS, Edwards JR, Beldavs ZG, et al. Prevalence of Antimicrobial Use in US Acute Care Hospitals, May-September 2011. *JAMA*. 2014; 312(14): 1438-46

- Polage CR, Gyorke CE, Kennedy MA, et al. Overdiagnosis of Clostridium difficile infection in the molecular test era. *JAMA Intern Med*. 2015; 175(11):1792.

- Solomon DA, Milner DA. ID learning unit: understanding and interpreting testing for Clostridium difficile. *Open Forum Infect Dis*. 2014; 1(1):ofu007–ofu007.

- Srinivasan A. Engaging hospitalists in antimicrobial stewardship: The CDC perspective. *J Hosp Med*. 2011;6(S1):S31–S33.

- Wenzler E, Mulugeta SG, Danziger LH. The Antimicrobial Stewardship Approach to Combating *Clostridium Difficile*. Chang Y-F, ed. *Antibiotics*. 2015; 4(2):198-215.

Speaker Notes

Welcome to the "Antibiotic and Lab Stewardship to Prevent *Clostridioides difficile* Infections (CDI)" module. This module will provide an overview of antibiotic stewardship aspects and how they play a role in preventing CDIs and will discuss lab stewardship.

Speaker Notes: Slide 2

This module was developed by national infection prevention experts devoted to improving patient safety and infection prevention efforts.

At the end of this module you will be able to explain the mechanisms by which antibiotic stewardship impacts *C. difficile* infections, describe examples of how implementing the core elements of antibiotic stewardship programs prevents *Clostridioides difficile* infections, explain that *C. difficile* is a clinical diagnosis with no best diagnostic test and outline the role of diagnostic testing stewardship in preventing *C. difficile* infections.

A survey done in 2011 indicated that half of patients admitted to 183 hospitals in the United States were being treated with an antibiotic. Furthermore, several studies indicate that 30-50 percent of antibiotics prescribed in hospitals are unnecessary or inappropriate. This potentially inappropriate and avoidable exposure to antibiotics is the single most important risk factor for developing a *C. difficile* infection or CDI.

You should recall from the first module in this course, that it is part of the Tier 1 interventions to improve *C. difficile* infection rates at your institutions; antibiotic stewardship is inextricably linked to *C. difficile* infection and its prevention.

There are several proposed mechanisms explaining the relationship between *C. difficile* infection and antibiotic stewardship. The one that is probably best understood is on the individual level. Patients who are admitted to the hospital and get exposed to *C. difficile* can also go on to develop asymptomatic C*. difficile* colonization or *C. difficile* infection.

Antibiotic exposure causing disruptions to patients' microbiota, acquisition of a particularly toxigenic strain of *C. difficile* and failure to mount an immunological response all play a role in patients developing a full *C. difficile* infection. Antibiotic stewardship programs help individuals by avoiding inappropriate antibiotics, thereby reducing the risk of that patient becoming infected with *C. difficile*.

Antibiotic stewardship also reduces *C. difficile* infections at the unit and even hospital level. Numerous patients in the acute care setting already have asymptomatic *C. difficile* colonization. If they are exposed to antibiotics, they can develop antibiotic-associated diarrhea independent of their *C. difficile* colonization. This diarrhea results in shedding of *C. difficile* spores that then contaminate the environment. These spores in the environment can then go on and expose *C. difficile* naive patients, further cascading to several *C. difficile* infections on a unit, ward or hospital.

Speaker Notes: Slide 6 Continued

Antibiotic stewardship disrupts this process early on by preventing inappropriate antibiotic exposures, reducing diarrhea and environmental contamination. Reducing the number of patients at risk from loss of good bacteria, to ultimately prevents *C. difficile* infections.

In this way, antibiotic stewardship can have a multiplicative effect on rates of *C. difficile* infections at a facility.

Speaker Notes: Slide 7

Let's look more closely at how hospitals can improve their antibiotic stewardship programs to specifically improve CDI.

In 2014 the Centers for Disease Control and Prevention, or CDC, described the core elements of antibiotic stewardship programs in an effort to help acute care hospitals improve antibiotic use.

The CDC recommends that every antibiotic stewardship program have seven core elements. They include: leadership commitment, accountability, drug expertise, actions to improve use, tracking, reporting and education. This module will review how certain elements should be targeted to reduce CDI rates.

Due to the time, effort and expertise required to implement and maintain a successful antibiotic stewardship program, leadership commitment is crucial. In order to make a pitch to financially-minded leadership, consider putting together a business case and highlight the return on investment of incorporating CDI-specific elements into your antibiotic stewardship program.

Include a focus on the idea that efforts to reduce CDI can often pay for themselves through savings. This includes direct savings through decreased antibiotic costs and indirect savings through decreased costs of caring for patients who will subsequently not develop CDI.

38

Speaker Notes: Slide 9 Continued

Each healthcare-associated CDI is associated with an average additional 12 days in the hospital and an increased estimated marginal cost of $29,000.

Getting your leadership on board can greatly increase your program success and get you much needed support. For more information about putting together a business case, consider reviewing the modules from a Business Case for Infection Prevention Course.

Speaker Notes: Slide 10

In addition to getting hospital leadership on board it is important to identify specific leaders to spearhead your antibiotic stewardship program. This should include a particular focus on CDI rates and prevention. A physician with training in infectious disease or quality improvement paired with an engaged pharmacist are common choices to fill these leadership roles. Leadership should be charged with improving both antibiotic stewardship processes, such as antibiotic use, as well as outcome metrics, specifically CDI rates.

Speaker Notes: Slide 10 Continued

One barrier that many facilities face is the lack of an available infectious diseases physician to take on this responsibility. It is important to realize that other types of physicians can also fill this leadership role. Hospitalists at many facilities are increasingly taking the lead in a variety of quality improvement (or QI) initiatives and are well suited to move stewardship efforts forward given their focus on QI and patient safety. Beyond this, an off-site or "remote" leader could also be an option to consider. Of course ultimately, every member of the health care team is responsible!

There are several key actions that can be part of your antibiotic stewardship program to specifically target CDI. Most importantly, your program should focus on supporting optimal antibiotic use to reduce unnecessary exposure to broad spectrum antibiotics and tailoring of ongoing antibiotic use based on the latest clinical data and lab results. Specific actions can be divided into three main categories: broad interventions that occur across a unit, service or facility; specific interventions focused on particular infections or antibiotics; and pharmacy- or lab-driven interventions that are built into the ordering system.

As you consider which actions to take to improve CDI and antibiotic stewardship at your facility, it is important to reflect on the characteristics of your hospital or unit that may influence implementation success. For example, what are the underlying issues at your facility that are driving increased CDI rates? What are unique characteristics of your facility or patient population that may impact program implementation? What is the institutional culture? Some facilities may be resistant to broad, sweeping changes, so starting on a smaller scale may help initiate change.

What about timing? Some interventions require significant lead time, but can pay long-term dividends, while other actions might be easier to implement but have less of a lasting impact. Lastly, facilities should avoid implementing two actions and interventions simultaneously. This may spread resources too thin and lead to staff confusion and resistance. For more information about important adaptive strategies to consider, review the Strategies for Infection Prevention Course.

Now that we have discussed more general antibiotic stewardship strategies to improve CDI, let's look at how some actual hospitals have enacted interventions to make improvements. We'll start with an example that was published earlier this year. A community hospital in Canada was interested in bringing down their rather high healthcare-associated CDI (HA-CDI) rates. A dedicated group of physicians and pharmacists focused on two specific antibiotics that have been associated with increased rates of CDI.

Speaker Notes: Slide 12 Continued

The action they took was to do real-time audit and feedback by a pair of infectious diseases physicians <u>and</u> pharmacists, to provide recommendations for potential changes to antibiotic regimens that included these two agents. Providing this feedback over the course of a few months resulted in an overall reduction of HA-CDI rates by 52 percent.

This is just one example of how a tried and true audit and feedback system can make a significant impact.

Let's look at another example that did not require the support structure of having an infectious diseases physician and pharmacist. This study took place at a large community hospital in Toronto after they had two hospital-wide CDI outbreaks. This hospital used a microbiology lab-driven intervention. They targeted ciprofloxacin given the association with CDI, and the intervention was to NOT automatically report Enterobacter sensitivity to ciprofloxacin unless it was resistant to other antibiotics. After doing this, they noted an overall 55 percent reduction in the use of ciprofloxacin. This is a good example of the potential impact of thoughtful changes that do not necessarily require a large team with many resources.

Let's look at a case to see how a number of different antibiotic stewardship actions can work together to help direct clinicians improve their antibiotic use.

Ms. Anderson is a 68-year-old woman with diabetes and hypertension who was admitted to the hospitalist service with a fever, productive cough and a new oxygen requirement of 2 liters. The emergency department diagnosed her with community-acquired pneumonia, or CAP. She was admitted for further evaluation and management.

Now the question to answer is, what is the "best" antibiotic regimen to treat her pneumonia?

Speaker Notes: Slide 15

Looking at the 2007 Infectious Disease Society of America, or IDSA, and American Thoracic Society, or ATS, guidelines, it is recommended that patients with community-acquired pneumonia admitted to the non-ICU setting be treated with a respiratory fluoroquinolone, or a Beta-lactam antibiotic plus a macrolide. Now it was drilled into me and many other physicians from an early age in medical school and residency that ceftriaxone and azithromycin is wonderful coverage for patients with CAP. The admitting physician knows this and wants this patient to improve, so the patient is started on ceftriaxone and azithromycin. Sputum cultures have been ordered, but have too much flora to be useful and the patient clinically improves.

Here at my hospital, the hospitalist service has partnered with the clinical pharmacist to have an: "antibiotic time-out" every Monday, Wednesday and Friday. The next day for this case happens to be a Wednesday, so at the time-out the clinical pharmacist weighs in and says:

Speaker Notes: Slide 16 Continued

"We have updated our CAP guidelines to reduce the use of fluoroquinolones and third generation cephalosporins, which place the patient at the highest risk for acquisition of *C. difficile* infection. We have had a rather high rate of CDI at our institution. Evaluation of the root cause for some of the CDI found an association with third generation cephalosporins such as ceftriaxone, which has been confirmed by other studies. Therefore our institutional guidelines, which are easily accessible on the web page and through our CPOE, have recently been changed to discourage such antibiotic use."

As a result of this discussion, the patient's antibiotic regimen is changed to ampicillin-sulbactam plus azithromycin and the duration of treatment is determined to be five days.

This example demonstrates how the combination of having the new institutional guideline for community-acquired pneumonia as well as having the antibiotic timeout to draw attention to those guidelines helped to improve antibiotic use. It is too soon to tell if these measures have had an impact on CDI rates at my institution, but this is a good example of a focused antibiotic stewardship intervention aimed at reducing CDI that uses a combination of different elements to achieve its goal.

Let us look at a potentially different path for this case. Say Ms. Anderson was treated with a prolonged course of a sub-optimal antibiotic for her pneumonia, specifically that she was treated with a full 14 day course of levofloxacin. She has dutifully taken all of her pills, and has shortly thereafter re-presented complaining with abdominal pain.

The question now is, should we be concerned enough about a possible infection that she should be tested for *C. difficile*?

The key thing to remember with *C. difficile* infection is that it is a clinical diagnosis. There are lab tests to help support clinical suspicion, but they must not be taken out of the clinical context.

A positive diagnostic test in the absence of supporting clinical information does not diagnose an infection. One of the reasons for this is the high rate of colonization. Studies indicate that up to seven percent of healthy adults have asymptomatic colonization with *C. difficile*, which rises to up to 15 percent of hospitalized adults and up to half of long-term care adults. In other words, just because tests indicate that *C. difficile* is present, this does not mean that it is causing an infection.

The patient needs to have clinical signs and symptoms of infection in order to know if this is a true infection and not colonization.

Ensuring that health care professionals are aware of these high rates of colonization will help them to realize that indiscriminate testing will lead to false positive results. Indeed, such over-testing likely is a driving factor in the high *C. difficile* rates at some institutions by mis-categorizing asymptomatic colonized patients as having *C. difficile* infections. Additionally, these false-positive tests can lead to inappropriate antibiotic use, which can further spread exposures as we discussed before.

The crucial symptom of *C. difficile* infection is clinically significant diarrhea with loose stools. In order to limit inappropriate testing, many institutions have their clinical laboratories set a threshold on the type of stool that is acceptable for *C. difficile* testing. The Bristol stool scale is a visual scale of stool density that progresses from type one which is described as "separate hard lumps, like nuts" to type seven which is described as watery, with no solid pieces, and entirely liquid. This scale can be used to standardize such an approach to *C. difficile* testing, but requires training of clinical lab personnel. On this scale, the recommended threshold for *C. difficile* testing is type five through seven.

Now rarely, a patient with *C. difficile* infection will have an ileus and complicated disease and will have a formed stool. This is a special clinical situation that requires provider communication with the clinical laboratory. Despite all of these measures, up to 50 percent of hospitalized patients tested for *C. difficile* do not have clinically significant diarrhea with loose stools, so clearly there is room for improvement.

Beyond testing only unformed stools, efforts should be made to ensure that there is no other explanation for the cause of the diarrhea. Studies indicate that between 19 to 40 percent of patients who are tested for CDI are currently receiving laxatives, which could further cloud the clinical picture.

Speaker Notes: Slide 19 Continued

Thus it is important to educate health care personnel on clinical features, transmission and epidemiology of CDI to help ensure appropriate testing. Testing of formed stool from asymptomatic patients is not clinically useful, including use as a test of cure. It is not recommended, except for epidemiological studies.

There is no "best" test to diagnose *C. difficile* infection. Tests vary by facility, and a variety of tests are available with different characteristics. It is important for clinicians to know which test they use at their facility and what it means.

ELISA tests to detect a *C. difficile* antigen called glutamate dehydrogenase, or GDH, that is produced by both toxin and non-toxin producing *C. difficile* strains. It is considered to be rather sensitive, but not very specific for toxin-producing *C. diff*. In other words, this test can help indicate if *C. diff* is present, but not if the bacteria are producing toxins which cause the disease.

ELISA tests to detect *C. difficile* toxins, both A or B, are commonly used. However, these tests are not very sensitive and miss up to 30 percent of cases. Both of these ELISA tests return rather quickly; results are typically available within one to four hours. PCR assays also rapidly detect the presence of *C. diff* toxins. However, they are expensive, and if they are used indiscriminately in patients who are not having clinically significant diarrhea with loose stools, they are likely to pick up colonized patients. Therefore, PCR assays should be used in conjunction with a good stool stewardship program. Currently, approximately 44 percent of acute care hospitals are using the PCR test either independently or in combination with other *C. diff* tests.

Speaker Notes: Slide 20 Continued

Given the variety of sensitivities and specificities for these tests, it is recommended to not automatically repeat a test if the prior test was negative unless the clinical situation indicates at least a medium pre-test probability (high suspicion) for CDI. To facilitate this, many clinical labs will not process duplicate specimens within a 24-hour period.

Cultures and cytotoxin assays can take up to 3 days to return a result, and therefore are not particularly useful in the clinical setting. Just as with stool sample analysis, exclusive reliance on molecular tests for CDI diagnosis without testing for toxins or host response is likely to result in over diagnosis, overtreatment and increased health care costs

It is important to balance being selective about which patients and what type of stool to test for *C. diff* with the need to quickly identify CDI by expedited testing. The longer it takes to identify patients with *C. difficile* infections, the greater the chance for environmental contamination and potential for healthcare-associated transmission to other nearby patients. Institutions should ensure that stewardship measures to enhance the appropriateness of *C. difficile* testing do not delay testing overall. Clinicians should be supported in their efforts to quickly identify high-risk patients and send *C. difficile* testing.

Speaker Notes: Slide 21 Continued

Some institutions with high rates of *C. difficile* infection implement early isolation techniques, so that patients are automatically placed into Isolation Precautions once a *C. difficile* test is sent. Other organizations train and empower the bedside nursing staff to recognize patients at high risk for *C. difficile* infection and to place them into Isolation Precautions before a provider even places an order for *C. diff* testing. On the back end, it is recommended to have early and automatic notifications of positive *C. difficile* test results sent to nursing staff and clinical providers to ensure prompt isolation and treatment.

Returning to the case of the 68-year-old lady with abdominal pain following a sub-optimal treatment regimen for CAP: in order to know if she "should" be tested for CDI, we need more clinical information. Providers need to seek this information out and use it to determine if she should be tested.

Specifically, we would need to know if she was having clinically diarrhea with loose stools of the Bristol stool type five through seven or if she has an ileus. If either is the case, given her previous antibiotic exposure, she would be considered to be at high risk for *C. difficile* infection. Her stool should be evaluated for potential empiric isolation.

Before wrapping up this module, let's discuss some potential barriers to implementing laboratory stewardship practices you might face and some potential solutions and countermeasures.

Just as with antibiotic stewardship it is important for diagnostic stewardship:

- Improve hand-off communication across levels of care and upon movement of patients.
- Use automated laboratory alerts to notify health care professionals and the infection prevention department if a patient tests positive for CDI. This will help isolate patients promptly .
- Develop multidisciplinary teams to implement consistent testing and isolation practices.
- And lastly, implement processes for early detection of CDI, can ensure patients with clinically significant diarrhea on admission are tested promptly for *C. diff*.

In summary, focused antibiotic stewardship interventions can prevent *C. difficile* infections in a variety of ways. *C. difficile* infection is a clinical diagnosis, and there is no one best diagnostic test. Early and targeted testing for *C. difficile* infection is crucial to lowering *C. difficile* infection rates.

No notes.

No notes.