Antimicrobial Stewardship Strategies to Prevent *Clostridioides difficile* Infections

Clostridioides difficile is the most frequently reported healthcare-associated pathogen in hospitals [1]. Antimicrobial exposure is the most important modifiable risk factor for *Clostridioides difficile* infection (CDI) when a patient is also exposed to the *C. difficile* bacterium or spores [2]. Antimicrobial stewardship programs (ASP) coordinate efforts to improve and measure appropriate antimicrobial use by optimizing selection, dose, duration and route of therapy [3]. **The HAI Program recommends hospital infection preventionists (IP) and ASP leaders collaborate to implement CDI prevention strategies.**

1. Establish CDI reduction goals for the ASP.

Reducing CDI should be a high priority when designing ASP interventions [3].

Recommendations:

- ❑ Prioritize ASP interventions by using CDI surveillance data to identify patient populations, hospital locations and service lines with highest CDI incidence.
- ❑ Track CDI incidence as a primary ASP outcome.
- ❑ Include the hospital infection preventionist as an active ASP participant.

2. Limit high CDI risk antimicrobial prescribing by promoting use of lower risk antimicrobials, minimizing the number of antimicrobials prescribed, and ensuring shortest effective duration of therapy.

Increased CDI risk is observed with increasing cumulative antimicrobial dose, number, duration, and spectrum of activity [4]. Broad spectrum antimicrobials, including fluoroquinolones (i.e., ciprofloxacin, levofloxacin, moxifloxacin) and cephalosporins (e.g., ceftriaxone, cefepime) are associated with higher risk of CDI [2]. Patients with reported allergies to beta-lactam antimicrobials (e.g., penicillin) frequently receive alternative antimicrobials and are at increased risk of CDI [5]. Hospital-based ASP interventions aimed at reducing use of broad spectrum antimicrobials have been shown to reduce hospital-onset CDI [6, 7]. The Infectious Diseases Society of America (IDSA) guidelines for ASP implementation [3] and CDI management [2] strongly recommend interventions designed to reduce the use of antimicrobials associated with high CDI risk.

Recommendations:

- ❑ Implement formulary restriction with preauthorization by requiring clinicians to obtain approval from the ASP or Infectious Diseases service before prescribing high-risk antimicrobials.
- ❑ Conduct prospective audit with feedback by engaging the clinician who has prescribed a high-risk antimicrobial to recommend a narrower spectrum alternative, limit the number of antimicrobials prescribed, and ensure the shortest effective duration of therapy.
- ❑ Ensure communication of antimicrobial indication and anticipated duration of therapy when patients transfer between health care facilities to avoid unnecessarily prolonged or duplicative antimicrobial therapy.
- ❑ Develop and distribute local treatment guidelines [8] or order sets for common infection syndromes (e.g., community-acquired pneumonia, urinary tract infection) that preferentially recommend lower CDI risk empiric antimicrobial options as first-line therapies, and shortest effective duration of therapy.
- ❑ Perform beta-lactam allergy assessments and penicillin skin testing for patients with reported beta-lactam allergy to reduce prescribing of high-risk antimicrobials.

3. Optimize CDI treatment and stop unnecessary antimicrobials in patients with new CDI diagnoses.

Timely and appropriate CDI treatment is necessary to improve patient outcomes, prevent complications, including recurrence, and reduce the risk of *C. difficile* transmission. Optimal CDI treatment includes cessation or avoidance of

non-CDI antimicrobial use wherever possible [2]. ASP interventions can improve adherence to CDI management guidelines [9].

Recommendations:

- ❑ Develop CDI order sets that include recommendations for appropriate diagnostic testing, empiric therapy, and CDI treatment.
- ❑ Receive alerts from the microbiology laboratory (or electronic medical record) for all positive *C. difficile* test results, audit patient medical records for appropriateness of treatment, and provide feedback to clinicians if CDI management is not in accordance with guidelines.
- ❑ Implement procedures to "flag" medical records of patients with risk factors or recent history of CDI for ASP audit with feedback, and alert clinicians to avoid antimicrobials if possible or prescribe lower-risk antimicrobials.

4. Incorporate stewardship of CDI diagnostic testing practices to improve accuracy of CDI diagnosis and surveillance data.

Sensitive diagnostic testing methods allow for rapid identification of patients with CDI, implementation of isolation precautions to prevent transmission, and prompt initiation of therapy to improve patient outcomes. If used inappropriately to test patients without signs and symptoms of CDI, tests are more likely to detect asymptomatic colonization with *C. difficile* [10] and result in potentially inappropriate CDI therapy and inaccurate surveillance data.

Recommendations:

- ❑ Ensure the laboratory implements a policy to reject *C. difficile* testing of formed stool.
- ❑ Develop and distribute testing algorithms to direct proper use of CDI testing. Recommend testing only patients with 3 or more diarrheal episodes in a 24-hour period. Prior to CDI testing of patients on laxatives, discontinue use for 24-48 hours and reevaluate symptoms prior to CDI testing.

1. Magill, S.S., et al., *Multistate point-prevalence survey of health care-associated infections.* N Engl J Med, 2014. **370**(13): p. 1198-208.
2. McDonald, L.C., et al., *Clinical Practice Guidelines for Clostridium difficile Infection in Adults and Children: 2017 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA).* Clinical Infectious Diseases, 2018: p. cix1085-cix1085.
3. Barlam, T.F., et al., *Implementing an Antibiotic Stewardship Program: Guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America.* Clin Infect Dis, 2016. **62**(10): p. e51-77.
4. Stevens, V., et al., *Cumulative antibiotic exposures over time and the risk of Clostridium difficile infection.* Clin Infect Dis, 2011. **53**(1): p. 42-8.
5. Macy, E. and R. Contreras, *Health care use and serious infection prevalence associated with penicillin "allergy" in hospitalized patients: A cohort study.* J Allergy Clin Immunol, 2014. **133**(3): p. 790-6.
6. Feazel, L.M., et al., *Effect of antibiotic stewardship programmes on Clostridium difficile incidence: a systematic review and meta-analysis.* J Antimicrob Chemother, 2014. **69**(7): p. 1748-54.
7. Baur, D., et al., *Effect of antibiotic stewardship on the incidence of infection and colonisation with antibiotic-resistant bacteria and Clostridium difficile infection: a systematic review and meta-analysis.* Lancet Infect Dis, 2017.
8. *Johns Hopkins Antibiotic Guidelines - Treatment Recommendations for Adult Inpatients*. 2015-2016 [cited 2017 October]; Available from: http://www.hopkinsmedicine.org/amp/guidelines/Antibiotic_guidelines.pdf.
9. Jury, L.A., et al., *A Clostridium difficile infection (CDI) stewardship initiative improves adherence to practice guidelines for management of CDI.* Infect Control Hosp Epidemiol, 2013. **34**(11): p. 1222-4.
10. Dubberke, E.R., et al., *Strategies to prevent Clostridium difficile infections in acute care hospitals: 2014 Update.* Infect Control Hosp Epidemiol, 2014. **35**(6): p. 628-45.