

Clostridium difficile Infections: Diagnosis, Treatment, and Prevention

Focus of Research for Clinicians

A systematic review of 102 clinical studies published from December 1978 to August 2011 examined the comparative effectiveness of diagnostic tests, treatments, and prevention strategies for *Clostridium difficile* infections (CDIs) in adults. The review did not include an evaluation of other causes of antibiotic-associated diarrhea. This summary is provided to inform discussions of options with patients and to assist in decisionmaking along with consideration of a patient's values and preferences. However, reviews of evidence should not be construed to represent clinical recommendations or guidelines. The full report is available at www.effectivehealthcare.ahrq.gov/cdiff.cfm.

Background Information

CDIs are a growing health care problem in hospital, outpatient, and long-term care facilities. In 2005, approximately 250,000 hospitalizations were associated with CDI. While culturing and testing for toxin remains the gold standard for diagnosing CDI, the demands for rapid results have led many laboratories to rely on immunoassays that detect the presence of toxins in stool samples and, more recently, genetic tests that detect toxin-related genes. The comparative effectiveness of these various tests has not previously been reviewed.

FDA-approved antibiotics for the treatment of CDI include oral vancomycin and fidaxomicin. However, concerns about antibiotic overuse, increasing pathogen resistance, and cost have led to the use of other antibiotics such as metronidazole to treat mild-to-moderate CDI. Metronidazole and vancomycin are the two most commonly used treatments, but they are ineffective in 8 to 36 percent of patients with primary CDIs, and there are no antibiotics that kill *C. difficile* spores. Also, relapse or recurrence occurs in 20 to 25 percent of patients. For these reasons, there is interest in the comparative effectiveness of current antibiotic treatments for CDI, the use of nonstandard interventions for multiple recurrences, and prevention strategies.

Conclusions

The limited evidence on the comparisons of immunoassays and genetic tests do not provide guidance to change current diagnostic approaches. Comparisons of oral vancomycin and metronidazole as well as vancomycin and fidaxomicin demonstrate similar initial cure rates. However, fidaxomicin is associated with significantly lower recurrence rates than vancomycin for patients infected with non-NAP1 strains of *C. difficile*. For patients with the NAP1 strain, recurrence rates did not differ by treatment. For patients with multiple recurrences, use of *C. difficile* immune whey or fecal flora

reconstitution show promise, but evidence is low. Limited evidence supports current practices for prevention, including appropriate antibiotic stewardship to reduce the use of broad-spectrum antibiotics.

Clinical Bottom Line: Diagnosis and Treatment

Diagnostic Tests

- Limited evidence suggests that sensitivity and specificity of commercially available toxin A and B immunoassays are not significantly different; newer genetic tests may increase sensitivity, but may lose specificity. ●○○

Treatment With Antibiotics

- Initial cure rates are similar for oral vancomycin versus metronidazole and vancomycin versus fidaxomicin. ●●○ (No head-to-head trial demonstrated superiority of any single antimicrobial for initial clinical cure, recurrence, or mean days to resolution of diarrhea.)*
- Recurrence rates were about 10 percent lower after treatment with fidaxomicin when compared with vancomycin (15% vs. 25%; $P = 0.005$). ●●○
- Patients treated with vancomycin for a non-NAP1 strain infection were about 3 times as likely to have a recurrence than patients treated with fidaxomicin, but patients with the NAP1 strain had recurrence rates that did not differ significantly by treatment. ●○○

* Antibiotic comparisons included: vancomycin versus nitazoxanide, bacitracin, and high-dose vancomycin; and metronidazole versus nitazoxanide. Metronidazole was also compared to metronidazole plus rifampin with no evidence of superiority but with a statistically significant higher mortality associated with the combination (5% vs. 32%; $P = 0.04$).

NAP1 = North American Pulsed Field type 1 strain.

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Strength of Evidence Scale

- High: ●●● There are consistent results from good-quality studies. Further research is very unlikely to change the conclusions.
- Moderate: ●●○ Findings are supported, but further research could change the conclusions.
- Low: ●○○ There are very few studies, or existing studies are flawed.
- Insufficient: ○○○ Research is either unavailable or does not permit estimation of a treatment effect.

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Nonstandard Treatment and Prevention for Multiple Recurrences

- Adding probiotics containing certain *Saccharomyces* spp. to antibiotics for primary treatment may increase the risk for fungemia-related complications in critically ill patients and adds no known benefit. ●○○
- *C. difficile* immune whey is well tolerated and is similar to metronidazole for treating recurrent CDI. ●○○
- Fecal flora reconstitution via fecal transplantation prevents recurrent infections for up to 1 year. ●○○
- Probiotics, prebiotics, and toxin-neutralizing antibodies alone do not reduce primary hospital CDI incidence rates. ●○○
- CDI recurrence rates were reduced three-fold when an oligofructose prebiotic ●○○ or toxin-neutralizing antibodies ●●○ were added to standard antibiotics.

Clinical Bottom Line: Prevention of Primary and Recurrent CDI

- Appropriate antibiotic prescribing practices that decrease the use of high-risk antimicrobials may lower CDI incidence rates. ●○○
- CDI incidence may be reduced by using disposable gloves and thermometers and by disinfection with chemicals that kill *C. difficile* spores. ●○○
- Risk factors for CDI include antibiotic use, severe underlying disease, acid suppression, hospitalization in an ICU, age, and nonsurgical gastrointestinal procedures. ●○○

Evidence for Harms

- Harms were not reported with sufficient detail to compare the risk of any particular antibiotic with another. When harms were reported, they were generally not serious (e.g., nausea, emesis) and were transient.
- Harms related to prevention strategies (e.g., exposure to toxic chemicals, limited adherence, increased costs, and possible harm to surfaces) have not been studied.

Gaps in Knowledge

- Newer DNA-based diagnostic assays have promising initial results; however, it is not clear how differences in diagnostic test sensitivity and specificity affects clinical decisions and patient outcomes.
- Research is needed to determine the optimal institution-wide prevention strategies for addressing multiple potential routes of transmission and reducing patient susceptibility.
- Research is needed to determine if nonantibiotic interventions, such as probiotics, prebiotics, toxin-absorbing compounds, and fecal flora reconstitution, among others, can be effective in preventing primary or recurrent CDI.
- Limited available evidence suggests that oral vancomycin may provide higher initial cure rates for severely ill patients; however, more research in this patient population is necessary.
- A consensus definition is needed of CDI diarrhea (i.e., number and consistency of stools) that meets both clinical and research-oriented requirements.
- No included studies determined if hand washing was more effective than use of alcohol gels to reduce CDI incidence; however, *C. difficile* spores are known to be resistant to alcohol-based handrubs and other routinely used antiseptics.

What To Discuss With Your Patients

- What risk factors they may have that makes them or someone they care for susceptible to CDI.
- If they or someone they care for has CDI, how they can help prevent the spread of infection.
- Which antibiotic treatment is appropriate for their CDI.
- Whether or not nonstandard interventions would be beneficial especially considering their availability and potential costs to the patient.

Resource for Patients

Treating and Preventing C-diff Infections: A Review of the Research for Adults and Their Caregivers is a free companion to this clinician research summary. It can help patients talk with their health care professionals about treatment for and prevention of CDI. It provides information about:



- Available treatments for CDI
- Ways to prevent the spread of CDI
- Questions for patients to ask their doctor

Ordering Information

For electronic copies of *Treating and Preventing C-diff Infections*, this clinician research summary, and the full systematic review, visit www.effectivehealthcare.ahrq.gov. To order free print copies, call the AHRQ Publications Clearinghouse at 800-358-9295.

Source

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