

Antibiotics and Clostridium *difficile* Disease

Antibiotic use is a major modifiable risk factor for *C. difficile* infection (CDI). All antibiotics are a potential risk but certain classes appear to be associated with higher risk. Even small amounts of antibiotics including surgical prophylaxis, can increase the risk of CDI. The highest risk for CDI occurs during the first two months post therapy. It takes up to three months of NO antibiotic therapy for CDI risk to return to baseline.

Number of Antibiotics prescribed	Hazard ratio
1	Reference
2	2.5 (1.6-4.0)
3 or 4	3.3 (2.2-5.2)
5 or more	9.6 (6.1-15.1)

Duration of Antibiotic Exposure	Hazard Ratio
<4 days	Reference
4-7 days	1.4 (0.8-2.4)
8-18 days	3.0 (1.9-5.0)
>18 days	7.8 (4.6-13.4)

Antibiotic Class	Example(s)	Hazard Ratio
Fluoroquinolones	Levaquin; Cipro	4.0 (2.7-5.9)
3rd & 4th generation cephalosporins	Rocephin; Cefepime	3.1 (1.9-5.2)
Vancomycin	Vancomycin	2.6 (1.7-4.0)
1st & 2nd generation cephalosporins	Cefazolin; cefuroxime	2.4 (1.4-4.1)
Beta-lactamase inhibitor combinations	Unasyn; Zosyn	2.3 (1.5-3.5)
Sulfas	Bactrim	1.9 (1.1-3.4)
Penicillins	Ampicillin; Nafcillin	1.9 (0.9-4.0)
Clindamycin	Clindamycin	1.9 (0.8-4.4)
Macrolides	Zithromax	1.5 (0.7-3.1)
Aminoglycosides		0.9 (0.3-3.0)
Metronidazole	Metronidazole	0.3 (0.1-0.9)
Miscellaneous	teracyclines; nitrofurantoin; others	1.3 (0.7-2.6)

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Other risk factors influencing the increased risk of CDI include:

- Antacid use
- Proton pump inhibitor use
- Inflammatory bowel disease
- Immunosuppression from medications associated with organ transplant
- End Stage Renal Disease (ESRD)
- Tube feeding
- Chronic liver disease

Hospitalizations, including stay in long term care facilities, also influence risk of CDI. Long Term Care Facilities (LTCF) are estimated to be the source of 40% of CDI cases. The risk of is directly related to the duration of stay which increases with each additional day! Colonization rates can be:

- 13% with 1-2 weeks of hospitalization
- 50% with greater than 4 weeks hospitalizations

Additionally, the risk of acquiring CDI increases with age; about 2% for each year of age which is most strongly associated with age > 65 years.

Finally, immune responses to *C. difficile* toxins and genetics are predictive of exaggerated inflammatory response.