CLOSTRIDIUM DIFFICILE INFECTION (CDI)
Supporting information

This guideline has been prepared with reference to the following:

NICE. Faecal microbiota transplant for recurrent Clostridium difficile infection. 2022. London. NICE

https://www.nice.org.uk/guidance/htg638

NICE. Clostridioides difficile infection: antimicrobial prescribing. 2021. London. NICE

https://www.nice.org.uk/guidance/ng199

American College of Gastroenterology. Guidelines for Diagnosis, Treatment, and Prevention of Clostridium difficile Infections. 2021

http://gi.org/guideline/diagnosis-and-management-of-c-difficile-associated-diarrhea-and-colitis/

Does administration of an antimicrobial in the previous 3 months increase the risk of C. difficile Infection (CDI)?
A 2011 Dutch case-control study found that antibiotic use increases the risk for CDI during therapy and in the period of 3 months after cessation of antibiotic therapy (Stevens, 2011). The highest risk for CDI was found during and in the first month after antibiotic use. During antibiotic therapy and in the first month after cessation of the therapy, patients had a 7–10-fold increased risk for CDI (OR 6.7–10.4). This risk declined in the period between 1 and 3 months after the antibiotic was stopped (OR 2.7). All antibiotic classes, except first-generation cephalosporins and macrolides, were associated with CDI. Second- and third-generation cephalosporins (OR 3.3 and 5.3, respectively) and carbapenems (OR 4.7) were the strongest risk factors for CDI. Patients with CDI used more antibiotic classes and more defined daily doses, compared with non-diarrhoeal patients.
A retrospective Swedish study found that the time gap between antibiotic exposure and onset of CDI is markedly different between different antibiotics (Karp 2024). The authors concluded that decreased cephalosporin use could delay onset of healthcare facility-associated CDI and limit infections with onset within the hospital. Cephalosporins caused CDI faster (mean 7.6 days), and more often during ongoing antibiotic therapy (81% of the cases) than any other antibiotic group. All other common agents had between 2-3 times longer period between start of exposure to onset of CDI (quinolones more than 3 times).

Karp J, Edman-Wallér J & Jacobsson G et al. Duration from start of antibiotic exposure to onset of Clostridioides difficile infection for different antibiotics in a non-outbreak setting. Infect Dis (Lond). 2024;56:1049-56
https://cdn.ncbi.nlm.nih.gov/corehtml/query/egifs/https:--www.tandfonline.com-pb-assets-tandf-logos-tf_pubmed_OA_fulltext_icon.png

Stevens V, Dumyati G, Fine LS et al. Cumulative antibiotic exposures over time and the risk of Clostridium difficile infection. Clin Infect Dis. 2011;53:42-8
https://academic.oup.com/jac/article/67/3/742/794937

Evidence Level: 4

After a C. difficile Infection how long does it take for the diversity of normal gut flora to recover?
No evidence identified.

Which drugs other than antibiotics reduce the diversity of gut flora?
A large population-based study from the Netherlands showed that proton pump inhibitors were the drugs most associated to a decreased diversity in the gut microbiome (Imhann, 2016). Similar results showing a lower microbial diversity and lower abundance of gut commensals were observed in a study analysing data from faecal samples from 1827 twins (Jackson, 2016).
A 2020 review found evidence to suggest that metformin reduces the diversity of gut flora (Weersma, 2020). The same review also highlighted studies suggesting laxatives, statins, antidepressants and opioids, can explain some of the variability in gut microbiome composition.

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A 2021 review found that a wide range of anti-cancer drugs can modify and reduce the diversity of gut flora (Jaye, 2021).

Imhann F, Bonder MJ, Vila AC et al. Proton pump inhibitors affect the gut microbiome. Gut. 2016;65:740-8 https://gut.bmj.com/content/65/5/740.long

Jackson MA, Goodrich JK, Maxan ME et al. Proton pump inhibitors alter the composition of the gut microbiota. Gut. 2016;65:749-56 https://gut.bmj.com/content/65/5/749.long

Jaye K, Li CG & Bhuyan DJ. The complex interplay of gut microbiota with the five most common cancer types: From carcinogenesis to therapeutics to prognoses. Crit Rev Oncol Hematol. 2021;165:103429

Weersma RK, Zhernakova A & Fu J. Interaction between drugs and the gut microbiome. Gut. 2020;69:1510-9 https://gut.bmj.com/content/69/8/1510.long

Evidence Level: 3

Last amended October 2025
Last reviewed January 2026