

# The Appendix Is a Possible Ally Against *C. diff* Infections

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## Key Findings:

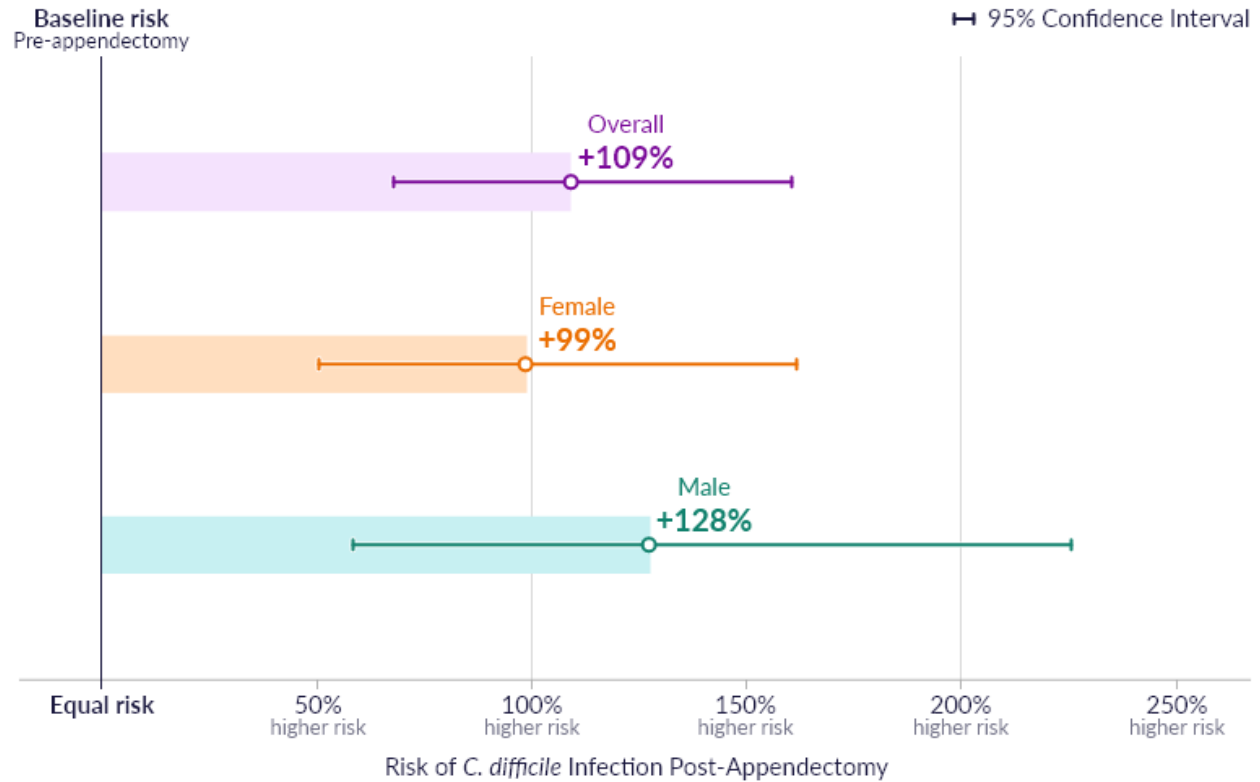
- Patients' risk of *Clostridioides difficile* (*C. diff*) infection is more than double after appendix removal compared to their risk prior to their appendix removal.

The appendix, a small organ within the gastrointestinal (GI) tract, has been a subject of medical curiosity due to its unclear function. Some research suggests that the appendix may serve an immunological role, acting as a reservoir for beneficial bacteria that can enhance GI flora.<sup>1</sup> To understand the potential correlation between the appendix and *Clostridioides difficile* (*C. diff*) infection, a GI infection that typically presents with symptoms such as diarrhea, nausea, abdominal pain, and fever,<sup>2</sup> we studied 57,225 patients who had their appendix removed (an appendectomy) between 2010 and 2021.

First, we compared the risk of overall GI infections in the six months to two years before an appendectomy to the six months to two years after an appendectomy. No statistically significant difference in risk was observed.

However, when looking only at the incidence of *C. diff* for this population, we found that the risk of *C. diff* infection is more than double—a 109% increase—after an appendectomy compared to that same patient's risk before the appendectomy, as seen in Figure 1. This correlation was slightly more pronounced for male patients with a 128% increased risk of *C. diff* infection after their appendectomy compared to an increase of 99% for female patients. Of note, only a small proportion of patients studied had *C. diff* infections both before and after the appendectomy.

## Clostridioides difficile Infection Risk Before and After Appendectomy



N=57,225 patients

"Clostridioides difficile Infection Risk Before and After Appendectomy," 2024. EpicResearch.org

Figure 1. The risk of developing a Clostridioides difficile infection after an appendectomy compared to before the appendectomy.

These data come from Cosmos, a dataset created in collaboration with a community of Epic health systems representing more than 246 million patient records from 1,400 hospitals and more than 32,500 clinics from all 50 states and Lebanon. This study was completed by two teams that worked independently, each composed of a clinician and research scientists. The two teams came to similar conclusions. Graphics by Aishwarya Shettigar.

### References

1. Randal Bollinger R, Barbas AS, Bush EL, Lin SS, Parker W. Biofilms in the large bowel suggest an apparent function of the human vermiform appendix. *J Theor Biol.* 2007;249(4):826-831. doi:10.1016/j.jtbi.2007.08.032
2. What is C. diff? Centers for Disease Control and Prevention. Published December 7, 2023. <https://www.cdc.gov/cdiff/what-is.html>. Accessed April 11, 2024.

### Data Definitions

Term	Definition
Study period	2010 to 2023
Study population	All patients with an appendectomy between 2010 and 2021.  Patients are required to have an encounter in each of the two years before and after their procedure, and one additional encounter after the follow-up period.

	Patients with a history of Crohn's disease, ulcerative colitis, IBS, or other immunocompromising conditions were excluded.
<b>Appendectomy</b>	A procedure with CPT code 44950, 44955, 44960, 44970, or 44979.
<b>Outcomes</b>	Presence of the following infection between six months and two years following the appendectomy, compared with rates between six months and two years prior to surgery.  Clostridioides difficile infection – A diagnosis with ICD-10-CM code A04.7*. GI infection – A diagnosis with ICD-10-CM code A00*, A01*, A02*, A03*, A04* (except A04.7*), A05*, A06*, A07*, A08*, or A09*.
<b>Crohn's disease</b>	A diagnosis with ICD-10-CM code K50*.
<b>Ulcerative colitis</b>	A diagnosis with ICD-10-CM code K51*.
<b>IBS</b>	A diagnosis with ICD-10-CM code K58*.
<b>Immunocompromising conditions</b>	Cancer – A diagnosis with ICD-10-CM code C*. HIV/AIDs – A diagnosis with ICD-10-CM code B20. Cystic fibrosis – A diagnosis with ICD-10-CM code E84*. History of transplant – A diagnosis with SNOMED code 77465005. History of splenectomy – A diagnosis with ICD-10-CM code Z90.81 or CPT code 38100, 38101, or 38102.

**Table 1: Clostridioides difficile Infection Risk Before and After Appendectomy**

Population	Outcome Group	Patients	Prior Infection	Prior Rate	Post Infection	Post Rate	Risk Ratio	CI Low	CI High
All	Viral Infection	90,307	799	0.88%	749	0.83%	0.94	0.85	1.04
All	Bacterial Infection	90,307	309	0.34%	342	0.38%	1.11	0.95	1.29
All	CDiff	90,307	118	0.13%	247	0.27%	2.09	1.68	2.61
Female	CDiff	52,812	75	0.14%	149	0.28%	1.99	1.51	2.62
Male	CDiff	37,486	43	0.11%	98	0.26%	2.28	1.59	3.26