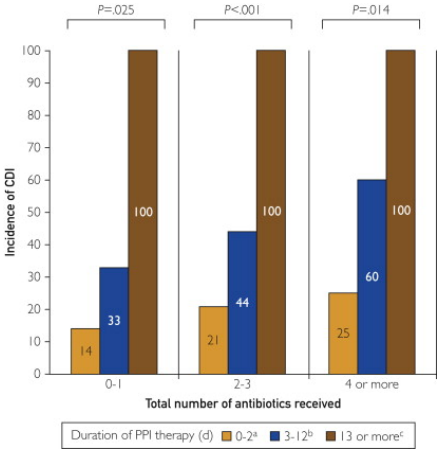
Proton-pump Inhibitors (PPIs): Pros and Cons

Proton pump inhibitors (omeprazole, esomeprazole, lansoprazole, pantoprazole, rabeprazole) are used widely in patients who are hospitalized. Although there are data supporting their use in stress ulcer prophylaxis, these data support use in very limited populations to prevent clinically important bleeding. The key groups included in those recommendations are patients:

- who are mechanically ventilated for 48 hours or more
- have a coagulopathy
- major trauma, burns >25-30% and/or severe head injury
- multiple organ failure
- major surgical procedures

Importantly, the incidence of bleeding in patients at risk was estimated to be between 2% and 6% in early studies, but has subsequently been shown to be much lower with a range between 0.1% and 4%. These recommendations have been extrapolated, for very unclear reasons, to use in many other inpatients leading to overuse of proton pump inhibitors. Overuse is important for several reasons including costs, the development of dependence on PPIs to prevent symptomatic dyspepsia, increased risk of pneumonia, osteoporosis, interstitial nephritis and an association with the development of initial and recurrent *Clostridium difficile* infection (CDI).

Potential biological mechanism of PPIs that may increase the risk of CDI includes decreased acid secretion in the stomach allowing for increased survival of spores, increased toxin production, effects on bile metabolism, and loss of maintenance of epithelial cell junctions. The data linking PPI use and CDI is not uniform, with some data supporting an association and some not finding a link.



Incidence of CDI in patients receiving a PPI, by duration of administration.

Proton Pump Inhibitors: B-II (8/8)

It has been reported that the use of PPIs leads to higher rates of CDAD [38]. PPIs cause a reduction in gastric acid production, but also potentially disrupt the intestinal microbiota, allowing *C. difficile* to overgrow. Gastric acid has an important role in eliminating the ingested non-spore-forming pathogens, but this role in eliminating *C. difficile* is speculative [38] (91).

A meta-analysis including 23 studies on 288 620 patients undergoing PPI treatment showed a 65% increase of CDAD cases in patients who were taking PPIs (risk ratio [RR], 1.69; 95% confidence interval [CI], 1.40–1.97; $P < .001$) [38]. This meta-analysis did not include an RCT, which is why this preventive measure is graded B-II, even with the numerous studies demonstrating the relation between PPI intake and CDAD incidence.

Moreover, recurrence of CDAD may be associated with PPI use, as suggested in an article reporting that 95% of the 20 patients in the relapse group were receiving long-term PPI therapy ($P = .029$), vs 74% of the 104 nonrelapsing patients [39].

Pathway to Prevention of Nosocomial *Clostridium difficile* Infection, Clinical Infectious Diseases, 2015

Recommendation Limit PPI use to the following groups:

- Patients admitted and already taking PPIs
- For stress ulcer prophylaxis in high risk groups (listed above)

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