

# Celecoxib plus a proton-pump inhibitor has a lower risk of recurrent upper gastrointestinal bleeding than naproxen plus a proton-pump inhibitor in patients who require aspirin for cardiovascular disease

## Question

In people who have cardiovascular disease requiring aspirin and previous upper gastrointestinal (GI) bleeding, does celecoxib plus a proton pump inhibitor (PPI) have a lower risk of recurrent upper GI bleeding than naproxen plus a PPI?

## The study

**Who?** The study included 514 people who required low-dose aspirin for cardiovascular disease, had previous upper GI bleeding with endoscopically confirmed healed ulcers, and required ongoing non-steroidal anti-inflammatory drugs (NSAIDs) for chronic arthritis pain. Patients were negative for H pylori infection or had successful eradication.

**What?** The study compared a cyclooxygenase-2-selective NSAID (celecoxib) plus a PPI with a non-selective NSAID (naproxen) plus a PPI. All patients received aspirin, 80 mg daily.

Celecoxib + a PPI	vs	Naproxen + a PPI
Celecoxib, 100 mg twice per day, plus esomeprazole, 20 mg once per day, for 18 months		Naproxen, 500 mg twice per day, plus esomeprazole, 20 mg once per day, for 18 months

## What the researchers found

**7 fewer people out of 100 taking celecoxib plus a PPI had recurrent upper GI bleeding compared with those taking naproxen plus a PPI. There was no difference in the number of cardiovascular events.**

## The bottom line

In people who have cardiovascular disease requiring aspirin and a history of upper GI bleeding, celecoxib plus PPI has a lower risk of recurrent upper GI bleeding than naproxen plus PPI.

## Summary of findings

**Celecoxib vs naproxen in people who have cardiovascular disease requiring aspirin and a history of upper GI bleeding**

Outcomes at 18 months	Rate of events with celecoxib plus a PPI	Rate of events with naproxen plus a PPI	Absolute effect of celecoxib
Recurrent upper GI bleeding	5.6%	12.3%	About 7 fewer people out of 100 had recurrent upper GI bleeding at 18 months
Cardiovascular events (myocardial infarction, stroke, or cardiovascular death)	4.4%	5.5%	No effect*

\*Although the rates for the 2 groups look different, the differences were not statistically significant—this means that the difference could simply be due to chance rather than due to the different treatments.

*This Evidence Summary is based on the following article:*

Chan FKL, Ching JYL, Tse YK, et al. **Gastrointestinal safety of celecoxib versus naproxen in patients with cardiothrombotic diseases and arthritis after upper gastrointestinal bleeding (CONCERN): an industry-independent, double-blind, double-dummy, randomised trial.** *Lancet.* 2017 Jun 17;389(10087):2375-2382. doi: 10.1016/S0140-6736(17)30981-9. Epub 2017 Apr 11. PubMed (<https://www.ncbi.nlm.nih.gov/pubmed/28410791?dopt=Abstract>)

## **My patient had upper GI bleeding due to an ulcer but requires aspirin for cardiovascular disease and has severe arthritis – which NSAID will minimize the risk of recurrent bleeding?**

### ***Concomitant NSAIDs and aspirin***

NSAIDs are a major cause of GI bleeding. While it is strongly recommended that NSAIDs be avoided in patients who have a history of ulcers, some patients have arthritis pain that does not respond to other forms of analgesia. The risk of recurrent bleeding is further increased if the patient also requires aspirin for cardiovascular disease. In these high-risk patients, it is unclear which NSAID should be chosen to minimize the risk of recurrent bleeding.

### ***What were the results, and can I apply them to my patients?***

In this randomized trial, the rate of recurrent upper GI bleeding was significantly lower with celecoxib (5.6%) than with naproxen (12.3%) when each drug was combined with a PPI. The study groups did not differ for patient-reported pain outcomes or cardiovascular events. However, it is difficult to know if these results are applicable to all patients because the definition for cardiothrombotic disease and objective measures of the severity of baseline arthritis pain were not provided.

### ***Were there any limitations?***

The primary limitation of this study was the lack of a placebo group (aspirin + PPI + placebo), and therefore the baseline risk of recurrent GI bleeding is unclear. Also, this was a single-center study with considerable rates of recurrent bleeding despite PPI (5-12%), which may limit external generalizability. Although the results suggest no difference in cardiovascular events, the study was not powered to assess this outcome. A recent large randomized study found no difference between celecoxib and naproxen for cardiovascular safety.<sup>1</sup> Finally, follow-up of 18 months may have been too short to detect differences in treatment-related mortality.

### **Doctor, I had a GI bleed in the past and I take baby aspirin for a previous stroke. Can I also take another anti-inflammatory medication for my joint pain?**

In general, anti-inflammatory medications, such as celecoxib or naproxen, can make you bleed again from the stomach or intestine. Celecoxib may cause less bleeding than naproxen, but the risk is still high (at least 5 out of every 100 patients will have another bleed). Acetaminophen (Tylenol) would be a safer choice. Do not take anti-inflammatory medications without speaking with your doctor first.

### **References**

1. Nissen SE, Yeomans ND, Solomon DH, et al. Cardiovascular safety of celecoxib, naproxen, or ibuprofen for arthritis. *N Engl J Med* 2016; 375: 2519-29.

